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# MODERN MEDICINE

## ITS THEORY AND PRACTICE

### IN ORIGINAL CONTRIBUTIONS BY AMERICAN AND FOREIGN AUTHORS

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VOLUME III

INFECTIOUS DISEASES (CONTINUED)—DISEASES OF THE RESPIRATORY TRACT

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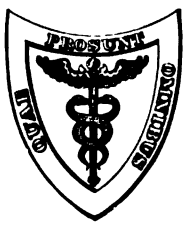


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# PART I.

# THE INFECTIOUS DISEASES—CONTINUED.

## CHAPTER I.

### MALTA FEVER.

By COL. DAVID BRUCE, C. B., F. R. S., D. Sc.

**Synonym.**—Mediterranean fever.

**Definition.**—A disease of long duration, characterized clinically by continued fever, profuse perspiration, constipation, frequent relapses, rheumatic or neuralgic pains, swelling of joints, or orchitis; bacteriologically, by the presence in the blood and organs of the *Micrococcus melitensis* (Bruce); and, anatomically, by congestion of the spleen and other organs.

**History.**—This fever has been elucidated chiefly by army medical officers, and its history may be briefly summed up as follows: The first paper of any importance was written in 1861 by Marston.[1] In it he described the fever from the clinical side very completely and clearly; and it will repay anyone interested in the disease to read his account. The next is by Veale,[2] in 1879, in which he describes the fever in patients invalided to England from Gibraltar, Malta and Cyprus. The next event of any importance was the discovery on July 9, 1887, of the specific organism of the disease, the *Micrococcus melitensis*.[3] Ten years afterward, in 1897, Wright and Semple applied the method of serum diagnosis to this fever, and this, especially in Malta, has helped greatly to distinguish this disease from other continued fevers. In this year, also, the late Surgeon-Captain M. Louis Hughes[4] published his lengthy monograph on *Mediterranean, Malta or Undulant Fever*, which contains everything known on the subject up to that date and also a full bibliography. Nothing more was done in the investigation of this fever until 1904, when a commission was formed, under the direction of the Royal Society of London, to continue the investigation. This commission

[1] *Army Medical Report*, 1863, vol. iii, p. 486.
[2] *Army Medical Report*, 1881, vol. xxi, p. 260.
[3] "Note on the Discovery of a Microörganism in Malta Fever," by Surgeon-Captain D. Bruce, *Practitioner*, vol. xxxix, 1887; and "The Micrococcus of Malta Fever," *Practitioner*, vol. xl, 1888; and "On the Etiology of Malta Fever," *Army Medical Report*, 1892, vol. xxxii, p. 365.
[4] *Mediterranean, Malta or Undulant Fever*, MacMillan & Co., 1897.

has been at work up to the present year (1907), and has furnished seven volumes of reports.[1]

**Geographical Distribution.**—This fever has been reported from *Spain*—Gibraltar; *Islands of the Mediterranean*—Balearic Islands, Corsica, Sardinia, Sicily, Malta, Gozo, Cyprus, Crete; *Italy*; *Greece*—Athens; *Turkey*—Constantinople, Smyrna; *Palestine*—Jerusalem; *Africa*—Tunis, Algiers, Alexandria, Suakin, Massowah, Zanzibar, Kimberley, Orange River Colony; *Arabia*—Aden; *India*; *China*—Hong Kong; *Pacific*—Philippine Islands, Fiji Islands; *North America*—Mississippi Valley; *West Indies*—Cuba, Porto Rico; *South America*—Venezuela, Brazil, Montevideo.

It is probable that many of these reported cases were not really Malta fever. The diagnosis was often made by the serum reaction to *Micrococcus melitensis*, a method which when used alone is apt to cause error. That the disease is a widespread one there can be no question, but it does not appear to occur in large numbers in any place except Malta, which is the home of this fever. It may also be said to be tropical and subtropical in its distribution, no cases, according to Hughes, having been reported north of 45° N. latitude, or south of 40° S. latitude.

**Distribution in Malta.**—Malta fever was thought at one time to be chiefly confined to the large towns of Malta, but now it is known to occur in every part of the island, and the disease is very prevalent in several of the inland towns and villages. The average incidence of the fever among the 200,000 Maltese is said to be about 30 per 10,000; whilst among the soldiers quartered in the island the incidence is about 370 per 10,000. In some years the incidence is double this, as, for example, in 1905 there were 643 cases of Malta fever among the soldiers alone (750 per 10,000) of whom 382 were invalided to England.

**Etiology.—The Micrococcus Melitensis.**—This coccus, or coccobacillus, is about 0.33$\mu$ in diameter, and usually occurs singly or in pairs, but when grown in broth appears in short chains. A bacillary form also occurs in cultures which have been grown at ordinary temperatures (18° C. to 20° C.). It is non-motile. It stains readily with all the basic aniline dyes, but loses its color rapidly when treated with alcohol or other decolorizing agent, and becomes unstained by Gram's method.

*Artificial Cultivation.*—Growth is extremely slow, and it is important that media which are faintly acid should be used. If markedly alkaline no growth whatever takes place. It shows a very slow and scanty growth at a temperature of 18° C., growing best at about 37° C. or 38° C. At temperatures between 40° C., and 42° C. growth is suspended. Above 42° C. artificial growths die. It is aërobic, but also grows in a feeble way anaërobically. The chief cultural characteristics are as follows:

In 1 per cent. glucose peptone, there is growth, but neither acid nor gas is produced. The same want of reaction occurs with lactose, saccharose, and starch peptone.

In litmus milk there is no clotting, and the reaction becomes distinctly alkaline in a few weeks.

[1] *Reports of the Commission Appointed by the Admiralty, the War Office, and the Civil Government of Malta, for the Investigation of Mediterranean Fever, Under the Supervision of an Advisory Committee of The Royal Society*, Parts I, II, III, IV, V, VI and VII, London: Harrison & Sons, 1905–06–07.

On potato it grows well; the growth is moist, transparent, and the formation of chains is well marked.

*Growth in Broth.*—After two or three days the broth becomes turbid. If allowed to stand for some time there is a deposit of flocculi, but the fluid remains turbid, and there is no pellicle formation. Indol reaction is negative. No odor is produced.

*Growth on Gelatine.*—Does not liquefy.

*Growth on Agar-agar.*—Cultures made directly from the organs after death on this medium, if faintly alkaline, show no growth for about four days, if kept at 37° C., and seven days if kept at 25° C. On sloped agar the colonies when they do appear are small and transparent, and resemble drops of dew.

*Plate Cultivation.*—On ordinary agar at 37° C., after three days, under the microscope the colonies on the surface are round, with an even border. They are bright and transparent, with a slight brown tinge about the centre, and are finely granular. As they grow older they become browner in color.

The addition of 1 per cent. nutrose enhances and quickens the growth of the micrococcus. To separate it from a mixture of others, it is best to use a medium to which glucose, nutrose, and litmus are added. The fact that it does not ferment glucose, and renders milk and other media alkaline, is an important feature, while the addition of nutrose adds somewhat to its rate of growth. On such a glucose-nutrose-litmus agar, the colonies appear blue, whereas many of the streptococci found in urine, fæces, etc., ferment glucose and give the medium an acid reaction.

In regard to the diagnosis of this species of bacteria, Horrocks says that a microörganism which agglutinates with a specific animal serum in a high dilution, does not ferment glucose, renders milk alkaline without coagulation, and does not retain stain by Gram's method, may justly be regarded as the *Micrococcus melitensis*.

**Life of the Micrococcus Melitensis Outside the Body.**—*Vitality.*—It is fairly resistant when outside the body. The most important facts are that it will resist desiccation in dust or on dry fabrics for sixty to eighty days. It will live in tap- or sea-water for about a month. Even in urine which has become markedly alkaline it has been found alive after six days. Exposure to the sun kills it in a few hours.

*Habitat Outside the Human Body.*—No one has, up to the present, found this parasite in external nature. The writer wrote in 1887 that, on account of the high temperature required for its growth, the length of time which elapses before the colonies appear, and the absence of any well-marked morphological or cultural characteristics, the search for it outside the body will be very difficult, if not hopeless. Many efforts have been made to find it in the air of wards, in dust from infected rooms, in the water of the harbors, or in the soil. Examinations of these materials have been made by plate cultures and by inoculation into susceptible animals, but without result.

**How Does The Micrococcus Leave the Body?**—All examinations of expired air, sweat, saliva, and scrapings of skin of patients have failed to show that the organism leaves the body by any of these routes. The urine, on the other hand, frequently contains them, sometimes in enormous numbers, but, as a rule, they are not numerous, ranging from 3 or 4 to 300 or 400 per cubic centimeter. Kennedy, a member of the Mediterranean Fever Commission, reports that he made some three thousand observations on the urine and found the *Micrococcus melitensis* in 10 per cent. This, taken

in connection with the long-continued vitality and virulence of the organism in a dry condition, may be a factor in the spread of the disease, though it must be confessed that up to the present there is no direct proof of infection by naturally infected dust. This excretion in the urine may go on for a long time (two years) after the patient is convalescent, so that these microbes must be scattered broadcast over the whole of Malta. It has not yet been ascertained how many cases of Malta fever remain unidentified, but there can be little doubt that many do, and these add to the general contamination of the surface of the soil. Shaw[1] examined 525 dockyard laborers and found that 79, or 15 per cent., gave a distinct agglutination with the *Micrococcus melitensis*. Of these 79, a marked reaction was present in 22, who were accordingly selected for a detailed examination. In 3 of them the organism was recovered from both blood and urine, in 1 from the blood only, and in 6 from the urine only. All these men were up and about and in full work during the period of observation. Two were kept under observation and continued to pass large numbers of micrococci in the urine from June, 1905, until the end of 1906, and are probably still excreting them (1907).

Although the micrococci have only been directly observed in the fæces of man on one occasion, they probably also pass out of the body by way of the alimentary canal. Eyre found micrococci throughout the whole length of the intestine in artificially inoculated rabbits. Horrocks and Kennedy have also found them in the gall bladder of man.

A third way of leaving the body is by the milk, and this is by far the most important from the point of view of infection. Naturally, it is difficult to obtain evidence of this mode of excretion in patients, on account of the absence of lactation in patients who have Malta fever. During the summer of 1906, however, 3 women were examined and the micrococcus recovered from the milk of 2 of them.

Although these three modes of leaving the body are probably the most important, yet a fourth remains for discussion. The blood of Malta fever patients contains micrococci, not in large numbers as a rule it is true, but still in appreciable amount. Now, a mosquito takes in about four milligrams of blood at each feeding, and, therefore, it is quite possible for the mosquito to ingest this micrococcus with the blood. Horrocks and Kennedy did in fact isolate *M. melitensis* on four occasions from the blood contained in the stomach of mosquitoes caught in fever wards.

**How Does the Micrococcus Enter the Body ?**—The success of preventive measures probably hangs on finding the correct answer to this question. Does the virus enter by way of the alimentary canal, by the lungs, through mucous membranes, or through the skin ? In other words, is it conveyed from the sick to the healthy by means of food, water, milk, by the inhalation of dust, or is it injected through the skin by suctorial insects ?

In trying to frame preventive rules against an infectious disease it is evident that the important thing to strive for is the narrowing down of the paths of infection. In yellow fever, as long as it was believed that it could be spread by contact, infected clothes, food, water, etc., nothing could be done. The moment the mode of infection was narrowed down to a particular species of mosquito the problem of prevention was simple. In the same way with Malta fever: if it can be spread by contact, contamination of food or

[1] *Reports of the Mediterranean Fever Commission*, vol. iv, p. 8.

water, by the inhalation of dust, sewer air, etc., it will be impossible to do more than recommend the ordinary established rules of hygiene. But, on the other hand, if the mode of spread can be narrowed down to such a vehicle as milk or a mosquito, something rapid and dramatic in the way of prevention might be attempted.

*By Contact.*—Many experiments have been made on this point, as naturally, questions of segregation of the sick, evacuation and disinfection of infected barracks and rooms depend on this mode of infection. In 1904 two monkeys belonging to the Mediterranean Fever Commission took the fever naturally. They were both living close to affected monkeys, and it was supposed, and probably rightly so, that they had taken the disease from their neighbors. This was repeated as an experiment on several occasions with, as a rule, positive results. Experiments made in which the contact was limited, that is to say, in which infection by urine was excluded, never succeeded. It was therefore concluded that the monkeys probably took the disease by having their food contaminated with the urine of their neighbors; or it might possibly be by eating ectoparasites containing blood; and that, therefore, contact resolved itself into a feeding experiment.

As the chance of man having his food contaminated in this way is very remote, it is probable that very few cases of Malta fever arise in this manner.

At the same time, this mode of infection cannot be absolutely excluded, and the high incidence, according to Johnstone, among those who nurse Malta fever patients may possibly be due to insufficient care in the handling of the urine of the patients. But the fact that no case of Malta fever has ever been known to occur in England, at Netley or Haslar Hospitals, where thousands of patients with this fever have been treated, is proof that, in practice, contact as a factor in the causation may be almost put out of court.

*By Contaminated Dust.*—As the organism can retain vitality for a long time in a dry condition, it was thought probable that the infection might be conveyed from the sick to the healthy by means of dust. Dust contaminated with urine from Malta fever cases might be blown into the atmosphere and so be inhaled or swallowed. In order to put this to the test various experiments were made. At first, artificially contaminated dust was used. The dust was sterilized, then made wet with an emulsion of the organisms from agar cultures, and finally dried. Horrocks relates 2 experiments, in 1 of which this dust was blown about the cage, and in the other blown directly into the nose and throat. Both were successful. Shaw also describes 2 experiments of blowing contaminated dust about an air-tight box containing the monkeys, but both were unsuccessful. In 2 experiments by him in which the dust was blown into the nostrils, 1 remained negative, and 1 gave a positive result. Of 4 experiments in which he frequently dropped dust into the conjunctival sac, 2 were negative and 2 positive.

From these experiments it may be concluded that *artificially* contaminated dust may convey Malta fever to healthy animals. This is not proof, however, that this ever occurs naturally. Artificially contaminated dust contains myriads of the specific micrococci. Dust in nature can contain but few, seeing how sparse they are in the urine as a rule. The dust blowing about under natural conditions must rapidly dilute the micrococci to an extraordinary extent, so that we can only picture a micrococcus here and there in a great quantity of dust. The natural conditions can be more closely imitated if the dust is contaminated with Malta fever urine and not from a culture.

*By Dust Artificially Contaminated with the Urine of Malta Fever Patients.*—A urine containing micrococci was used to contaminate the dust. After drying, the infective dust was blown into the nostrils and added to the food of monkeys. Four experiments are reported by Horrocks, lasting from twelve days to two months, but in no case did infection occur. It is difficult to understand why this experiment did not succeed. The dust was infected by a urine containing exceptionally large numbers of the micrococci, and immediately dried. It was evidently added in fairly large quantities to the food, as three out of four animals suffered from severe vomiting and diarrhœa. Shaw also reports that he experimented on four monkeys in the same way, but did not succeed in conveying the infection in a single case. These experiments are much more severe than anything we can imagine occurring in nature, and tend to throw doubt on dust being an important factor in the spread of Malta fever.

*By Dust Collected from Suspicious Places.*—This is, of course, the crucial experiment as far as infection by dust is concerned. Judging from the non-success of the last series of experiments with urine-contaminated dust, it was little likely that this experiment would succeed. It was, however, necessary to make the attempt. Dust was collected from fever wards, from places where cases had occurred, from around urinals, etc., and blown about the cages and food of monkeys, or injected subcutaneously. Up to the present all these experiments have failed.

When one considers the numbers of ambulatory and convalescent patients who must frequently be excreting this organism in the urine, one is led to think that this must constitute a means of spreading the disease. At the same time there is no absolute proof that this is so; the micrococcus has never been recovered from urine-contaminated places, or from the dust of such places; nor has the disease been set up in any animal by artificial inoculation with material from such places. Theoretically, there seems to be danger from the scattering broadcast of such a virulent and resistant microbe, but it is possible that not a single case of infection occurs in this way. As sound practice, however, any sanitary measures which could be devised to prevent the fouling of the soil by infected urine would be advisable.

*By Way of the Alimentary Canal.*—It has been repeatedly demonstrated by experiment that a small quantity of a culture applied to a scratch, or injected under the skin, will give rise to Malta fever in man and monkeys. Also that dust or fluids containing the micrococci, if applied to the unbroken conjunctiva, nasal passages, pharynx, interior of the larynx and trachea of monkeys, will set up this fever.

This question of the micrococcus gaining entrance by way of the alimentary canal is important. It is most essential that it should be known without any shadow of doubt whether or not a man can take this fever by swallowing the micrococci in his food or drink. It would also be well to know if this mode of infection takes place readily and whether many micrococci are necessary or some particular state of the digestive organs. A careful study of the evidence must convince anyone that Malta fever can be conveyed to healthy animals by way of the alimentary canal. Many animal experiments were made by the commission to settle this point, with the result that it is abundantly proved that animals can be readily infected by contaminated food or drink. For example, a single drink of milk containing comparatively few micrococci almost certainly gave rise to the fever.

*By Mosquitoes or Other Biting Insects.*—All the various species of mosquitoes found in Malta, other biting flies, as Stomoxys, fleas, etc., were first fed on affected animals and then at various intervals of time on healthy monkeys. The results of numerous experiments go to show that although such a method of infection is not absolutely disproved, it can only be of very rare occurrence.

As the result of all these experiments it stands out fairly clearly that the *Micrococcus melitensis* is conveyed from the sick to the healthy by way of the alimentary canal and therefore by some infected food or drink. There is no reason to believe that contact, inhalation of infective dust, or biting insects, play any prominent role. Then, again, from a study of the epidemiology of the fever, no suspicion could be attached to the water supply or any particular foodstuff.

**Infection by Means of Goats' Milk.**—As part of an investigation of this sort, it is necessary to examine the various domestic animals to find out if any of them, through which man might be infected, are susceptible to the disease. The monkey was the only experimental animal known to take the disease naturally; but various others, such as the guinea-pig and rabbit, could be infected by various expedients.

Attention was directed to the goats, which are so numerous and so much a feature of every-day life in Malta, and which supply most of the milk used in the island. Healthy goats were injected subcutaneously with cultures of *Micrococcus melitensis*, and, although they showed no signs of fever or ill-health, an examination of their blood showed that the micrococci were living and growing. This remarkable and unlooked-for observation led to the examination of various herds of apparently healthy goats perambulating the streets, and supplying the inhabitants with milk, and the important discovery was made that about 50 per cent. were affected by the disease, and that 10 per cent. were actually excreting the micrococcus in their milk. Monkeys fed on milk from an affected goat, even for one day, almost invariably took the disease. At this time, curiously enough, an important experiment on the drinking of goats' milk by man occurred accidentally. This is the case of the S. S. "Joshua Nicholson." In 1905 this steamer shipped sixty-five goats at Malta for export to the United States of America. The milk was drunk by the captain and many of the crew, with the result that an epidemic of Malta fever broke out on board the vessel, almost everyone who drank the milk being infected. Even after the goats reached America and were placed in quarantine, a woman who drank some of their milk had the fever.

Here, at last, a mode of infection was discovered which explained many of the curious features in the epidemiology of Malta fever: The irregular seasonal prevalence and the number of cases during the winter months, when there are no mosquitoes and little dust. It is true there are more cases in summer, but this may be explained by the conditions being more favorable for the multiplication of the micrococcus, by more milk or cream being used for fruit, in ice-cream, etc., and by the lowering of health during the hot months. It would explain the large number of cases arising among patients in hospitals where milk is used largely. It would also explain the liability to attack of the officer being three times as great as the private soldier, since the former consumes much more milk than the latter. It would also explain the isolated epidemics which sometimes occur in institutions, or in messes, such

as that related by Johnstone, where a sergeants' mess was severely infected while the men living in the vicinity escaped.

**Result of Preventive Measures Directed against the Use of Goat's Milk.**—Preventive measures, as the result of the discovery of infection among the goats, were first begun in Malta in June, 1906. The result was very striking. In July, August and September, 1905, there had been 258 cases among the soldiers, whereas in the same months in 1906 the number fell to 26. It must also be mentioned that 1906 began badly, there being an average incidence of 31 per 1,000 for the first six months of 1906 against 27.6 per 1,000 for the years 1899 to 1905.

Another striking example of the benefit of this simple preventive measure is given in the case of the Naval Hospital, Malta. This is a fine modern building, situated in extensive grounds. In spite of these advantages it had been in bad repute, on account of the number of cases of Malta fever which occurred among the inmates. Almost every patient who remained for a few weeks in the hospital took the disease. The goats supplying the hospital with milk were examined and several found to be passing the micrococcus in their milk. The use of goats' milk was forbidden, and from that date not a single case of Malta fever has appeared in the hospital.

A still more striking proof is afforded in Gibraltar, where some years ago this fever was prevalent. Gradually it grew less and less and finally has quite disappeared. Horrocks, who investigated this point, found that Malta fever had disappeared from Gibraltar *pari passu* with the disappearance of Maltese goats.

Taking all these facts into consideration, there seems reasonable ground for the belief that nine-tenths of the cases of Malta fever which occur in Malta are due to infection by goats' milk, and for the hope that Malta fever will be driven out and 74,880 days of severe illness blotted out of the yearly medical reports of the army and navy. This, if brought about, will be a brilliant achievement in the annals of preventive medicine, and will once more demonstrate the value of experimental methods in the elucidation of the etiology of disease. It is too early to be quite dogmatic, but the prospect appears hopeful, and the result of next year's campaign against this fever will be awaited with some anxiety and much interest.

**Age and Sex.**—There are no statistics available at the present time to enable us to state whether age or sex has any bearing on the incidence. In former papers by the writer, the opinion was hazarded that any age is liable and that sex has no influence.

**Length of Residence.**—According to Johnstone,[1] the heaviest incidence is among soldiers during their first year's service in Malta, and the severity of incidence continues to decrease with length of residence.

**Mode of Prevalence.**—This is curious and must depend on some particular cause. The officers and their wives and families, living in large, well-ventilated, well-cared-for houses, suffer more frequently than the non-commissioned officers and men, living in crowded barrack rooms. The disease occurs over all the island. Water supply, sanitary arrangements, or their absence, do not seem to affect the incidence. Now that the discovery of the infection among the goats has been brought to light, this peculiarity in the mode of prevalence is explained.

[1] *Reports of the Mediterranean Fever Commission*, vol. ii, p. 33.

**Months and Seasons.**—Tables and curves have been constructed by Johnstone,[1] and others, showing the relation of Malta fever to temperature and rainfall. From these it is seen that there is a close correspondence between the temperature curve and the Malta fever curve. As Johnstone points out, the rise of the latter curve follows that of the former at an interval of about one month, which would be approximately sufficient to allow for incubation and notification if the incidence of the fever were directly dependent on the temperature of the air. The rainfall curve is, broadly speaking, the opposite of the temperature curve, but the relation of the fever to the rainfall does not seem to be as manifest as its connection with the temperature. It must be noted, however, that, although the number of cases which occurs during the wet winter months is much smaller than that which occurs in the summer months, yet the fever by no means dies out, but continues all the year round, there being, roughly, a third as many cases notified during February as in August. It is difficult to believe that this fever is mainly carried by means of dust, as has been advanced, if one-third as many cases occur in the depth of winter, in the rainy season, as occur during the rainless months of July and August.

**Incubation Period.**—It is impossible to state exactly what the period of incubation is. Johnstone, who has gone into this subject as fully as possible, provisionally states that the available data tend to suggest that the incubation period is about fourteen days. One case is reported by Bassett-Smith with an incubation period of two months, but it stands alone, and there is some evidence that cases have occurred in as short a time as six days after arrival in Malta. The subcutaneous inoculation of monkeys gives an incubation period of about five days, whereas if the disease is given by ingestion the inoculation period appears to be lengthened to about fifteen days.

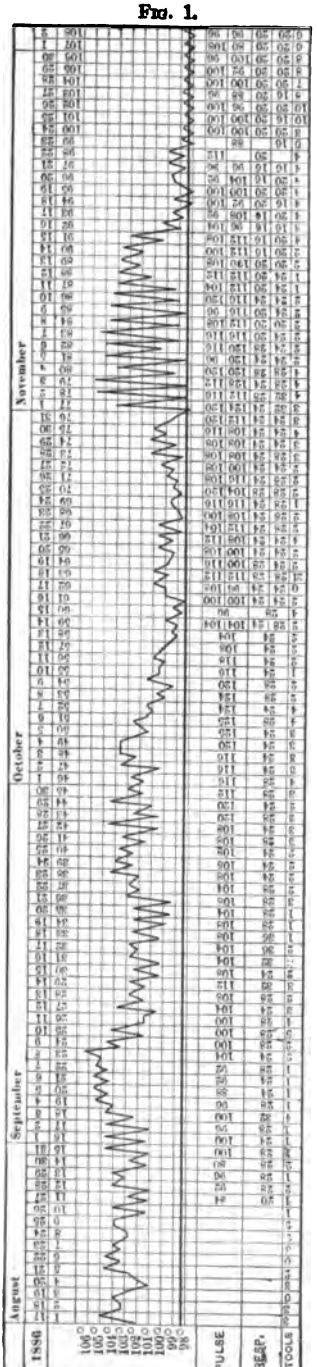
**Immunity from Second Attack.**—Although there is some diversity of opinion the writer's experience suggests that one attack of this fever does practically confer immunity. Lately, several monkeys which had recovered from the disease were reinoculated with a virulent culture and showed no reaction.

**Special Pathology.**—The anatomical changes are those due to high temperature and the circulation of toxins in the blood, and need not be described in detail. There is absolutely no specific inflammation of Peyer's patches, or other glands of the intestine. The spleen is always enlarged, averaging 20 ounces in weight. The mesenteric glands are only moderately enlarged, showing a marked contrast to typhoid fever. The lungs are always congested at the bases, but there is less liability to pneumonic consolidation than in typhoid fever.

**Symptoms.**—There is no great necessity to enter into the symptomatology at great length, as the symptoms are those commonly met with in other fevers, such as typhoid fever. There are, however, a few points which should be noted. For example, constipation is a marked symptom in Malta fever; in 65 cases, 48 are noted as being constipated throughout, whereas only 17 had diarrhœa at any time during the illness. The temperature curve must also be noted. On looking over a series of charts, the striking features are the extreme irregularity and the great tendency to relapses. The following chart may be taken as typical of a fairly severe attack of Malta fever, and from it can be judged the length and serious nature of the disease.

[1] *Report of the Mediterranean Fever Commission*, vol. ii, p. 35.

FIG. 1.




**Duration of the Fever.**—The average stay of soldiers in hospital is ninety days, but this does not represent the true average, as many of these men are invalided to England. Bassett-Smith gives the average duration in 50 cases at one hundred and twenty days. The length of this fever varies in different individuals between wide limits; while some return to duty within twenty or thirty days, on the other hand the writer has seen a case which lasted for more than three years.

Another important symptom is the pain and swelling of the joints. This complication occurs in nearly half the cases, and is very characteristic of the disease. Neuritis and orchitis come under the same category, and are fairly frequent. The orchitis is painful while it lasts, but usually passes away in a few days without leaving any bad effects.

**Sequelæ.**—There is little to be noted under this heading. Although considerable pain and inconvenience are caused by the swelling of, and effusion into, the joints, the arthritis usually clears completely and does no permanent damage. Neuritis is frequent in various nerves, and naturally tends to cause, in a few cases, prolonged anæsthesia, paresis, or even paralysis, of various regions and groups of muscles. In time these return to normal, and one can, as a rule, safely assure the patient of a return to complete health sooner or later.

**Mortality.**—The disease is not a very fatal one, 3 per cent. being the case mortality in the army during a period of seven years.

**Diagnosis.**—This is most important clinically in the distinction from typhoid fever, from which it differs chiefly in the longer duration, in the absence of rose spots, in constipation being the rule, in the frequent occurrence of painful arthritic or neuralgic symptoms, and, finally, in the much smaller rate of mortality. The surest method of diagnosis is the finding of the *Micrococcus melitensis* in the blood, *intra vitam*, or growing it from the spleen *postmortem*.

Shaw examined the blood of Malta fever patients on 51 occasions and found the micrococcus 30 times. His method was to draw off a few cubic centimeters of blood from a

vein of the arm and distribute it over several broth tubes. Zammit also was successful 27 times in 50 observations. He introduced a method which does away with the need of entering a vein. The finger or lobe of the ear is thoroughly cleaned and the dry skin is punctured with a needle. A sterile cotton-wool pad is used to remove the first drop of blood and an assistant squeezes the part for the next drop. A number of sterilized capillary tubes, one centimeter long, are ready in a test-tube. As soon as the drop of blood appears, one of these capillary tubes, held by sterilized forceps, is brought in contact with it, and when full, immediately dropped into a broth tube. Six tubes are usually filled.

If it is impossible to make a diagnosis in this way there remains the agglutination test. The writer must say that he has not as much confidence in this method of diagnosis as many profess to have. As one factor in the diagnosis it is valuable enough, but to trust to it alone is dangerous. It is a method which requires some experience to get good results. The personal factor comes in strongly; what is positive sedimentation to one observer is negative to another. Every examination of blood by this method should be safeguarded by control experiments. It must be borne in mind, for example, that the *Micrococcus melitensis* will give a positive agglutination reaction with almost all specimens of serum in dilutions of 1 in 2 and that blood taken from cases other than Malta fever will sometimes show signs of agglutination at 1 in 10, though this is the exception. A complete sedimentation is never obtained at 1 in 20 unless the blood is from a patient with Malta fever. The agglutinins may persist in the blood for long periods. It is reported that about 50 per cent. of patients will show the agglutination phenomenon two years after the illness in dilutions of 1 in 10, and one instance is reported as giving a positive reaction in a dilution of 1 in 20, seven years after recovery. This source of error must therefore be kept in mind.

One quality about the serum from patients with Malta fever is that if it does agglutinate the micrococci it does this in no uncertain way. The average dilution giving a complete reaction is given as 1 in 500, and cases have been reported up to 1 in 6,000. In regard to the time which elapses from the commencement of the fever to the appearance of the agglutinins in the blood, this is usually put down as occurring on the fifth day. As to the lowest dilution which may be accepted as proof of Malta fever, some workers put it at 1 in 10, if the clumping is well marked and takes place at once or within half an hour. In the writer's opinion 1 in 20 is a safer dilution.

**Prognosis.**—This is very favorable as regards life and ultimate recovery. The mortality seems to be somewhere between 2 and 3 per cent. If the patient tides over the first two or three weeks, he usually recovers. Death occurs, as a rule, in the first week or two of the disease, and is preceded by continued high temperature with a tendency to hyperpyrexia, delirium, dry tongue and diarrhœa. It is true that a patient sometimes dies at a later stage, the result of gradually increasing debility, but this is rare.

**Treatment.**—The essential points in prophylaxis are evident from the discussion of the etiology. Infection being frequent by the alimentary tract, every care should be taken to exclude all articles of food from the diet which may contain the causal organism.

In the treatment of this fever, there is no specific drug and the majority of patients are best treated by leaving out medicines altogether. Quinine is useless and salicylic acid and its derivatives equally so. The symptoms must

be treated on ordinary principles as they arise. The tendency to hyperpyrexia in severe attacks is one of the most important and dangerous of the symptoms and one of the most difficult to treat. It is doubtful if any real good is got from medicinal antipyretics, but careful watching and timely recourse to the cold bath may sometimes save life. Hydrotherapy is probably the most useful measure, sponges or baths being given. Sleeplessness, headache, arthritis and orchitis must be treated on ordinary principles.

# CHAPTER II.

## BERIBERI (KAKKE).

By MAXIMILIAN HERZOG, M. D.

**Definition.**—Beriberi—polyneuritis endemica (Baelz), neuritis multiplex endemica (Scheube)—may be defined as an acute, subacute or chronic infectious disease, characterized clinically by disturbances of the circulation, of motion and of sensation, and associated anatomically with hypertrophy and degeneration of the heart and degeneration of the peripheral nerves and of the voluntary muscles. Attention may be called primarily to the fact that clinically the disease varies considerably and that its etiology is still very incompletely understood. Hence, it is really almost impossible to give a concise, satisfactory definition of the disease, although the affection is undoubtedly an entity, and can be diagnosed as a rule without much difficulty. In Japan, which is the country where the disease is, or at least formerly was, most prevalent, and where it has been studied most extensively, both clinically and pathologically, the malady is known as Kakke.[1]

**History.—Geographical Distribution and Racial Predisposition.**—The first mention of beriberi is probably made in a work by a Chinese physician which appeared in the second century A. D., and a good description is to be found in a Chinese text-book on pathology, of the sixth century A. D. The first Japanese reports which mention the disease were written in the seventh and eighth centuries A. D. The disease is generally prevalent in tropical and subtropical countries, where the humidity is, as a rule, considerable. It is found in Asia—in Japan, including Formosa, in China, the Malay Archipelago and Peninsula, the Dutch possessions and in eastern India; it is also quite prevalent throughout the Philippine Islands. It occurs on the eastern coast of South America, particularly in Brazil, and a number of reports have come from Africa of its presence there during the last two decades. Some isolated epidemics have also occurred in England and Ireland, and sporadic imported cases have been encountered in Continental Europe, the United States and Canada.

Certain races are particularly susceptible to the disease, and wherever they travel are liable to disseminate it. This has been observed especially in the Japanese, the Chinese, and the Malays. The great prevalence of the disease in Japan has been emphasized by all writers on the subject. Baelz and K. Miura,[2] in their recent article on beriberi, state that probably 50,000 cases of beriberi occur each year in Japan. These figures, how-

[1] The disease is known by a variety of names in different countries where it is prevalent. For further information on the nomenclature and on the real or supposed etymology, the reader is referred to Scheube, *Die Beriberi-Krankheit*, Jena, 1894; and Scheube, *Die Krankheiten der warmen Länder*, Jena, 1903. An almost complete list of the very extensive literature of the subject will also be found there.

[2] Baelz and K. Miura, "Beriberi oder Kakke," *Mense's Handbuch der Tropenkrankheiten*, Leipzig, 1905, ii, p. 140.

ever, are much too low for the period of the late Russo-Japanese war, because during 1904, from February to December, more than 50,000 Japanese soldiers sick with beriberi were brought back from the field to the home country, while in the Japanese army at home for the same period of time several thousand cases more developed. These figures, it is to be understood, do not include any cases which occurred outside of the army among the general population.

**Etiology.**—In spite of the fact that the pathological anatomy is well known, the etiology is far from being definitely and satisfactorily understood. Wright,[1] in giving a summary of the theories regarding the etiology of the disease, mentions the following: (1) Gelbke's theory that beriberi is due to dry fish infected with a trichina; (2) M. Miura's theory that it is due to the ingestion of certain kinds of raw fish, principally combridæ; (3) Grimm's theory that it is due to the ingestion of infected fish; (4) Takaki's theory that it is due to a pathogenic diet in which nitrogen is deficient; (5) Ross' theory that it is due to arsenic poisoning; (6) the theory that it is due to the ingestion of mouldy rice; (7) Braddon's theory that it is due to the ingestion of a specific organism which develops on growing rice; (8) Manson's theory that it is due to a place germ (earth, floor or house) which distils a toxin, volatile or otherwise, that, being inhaled or ingested, produces the disease; and (9) Glogner's theory that it is due to a plasmodium. Other theories as to the etiology are that it is an anæmia of a pernicious type, that it is a modified and secondarily changed form of scorbutus, that it is due to carbon monoxide poisoning, that it is caused by *Ankylostomum duodenale* or by *Trichocephalus dispar*.

Without going into details we may say that not a single one of these hypotheses is tenable. Some of them even lack the very semblance of any support. Many cases of beriberi occur in well-nourished strong individuals, and the blood examination in acute or recent cases shows neither pernicious anæmia nor any anæmia at all. The author has examined the blood in a number of acute and chronic cases and has found no characteristic blood changes, although the cases of longer standing may show a varying degree of secondary anæmia.

While diet, and particularly a more exclusive rice diet, may act as a predisposing factor, it cannot be a determining and final factor, because the disease occurs also in countries or under conditions where little or no rice is consumed. The same is true with reference to fish. Experiments made on a large scale on several hundred prisoners for a period of eleven months caused Wright to conclude that, even though the diet be qualitatively and quantitatively correct, beriberi may nevertheless be contracted. He thinks that these experiments positively eliminate diet as a factor in the causation.

A number of investigators have laid claim to the discovery of a specific microörganism for the disease, as DeLacerda, Taylor, Rost, Ogata (bacilli), Van Eecke (a coccus), Pekelharing and Winkler (a bacillus and coccus), Wright, Dangerfield (cocci), Glockner (an amœba) and Fajardo (a hæmatozoön).

Durham[2] made some extensive experiments in order to ascertain if it was possible to infect monkeys, guinea-pigs and rabbits with beriberi. His experiments included the feeding of dried fish and rice, biting by bedbugs, injection of serum from beriberi patients, the feeding of the gastro-

[1] *An Inquiry, etc., into Beriberi*, Singapore, Kelly and Walsh, May, 1902.
[2] *Journal of Hygiene*, 1904, iv, No. 1, p. 112.

intestinal contents of patients to monkeys, the administration of dust from infected localities to monkeys, and throat to throat infection in these animals. All his experiments were absolutely negative.

The most recent claim to the discovery of a specific germ for beriberi is made by Okata and Kokubo, two Japanese army surgeons, who have had an excellent opportunity to study the most extensive beriberi material among the Japanese soldiers transferred from Manchuria to Japan during the recent Russo-Japanese war. These investigators have isolated a coccus, which generally assumes the form of a diplococcus and which may also at times present itself as a staphylococcus. They confidently maintain that this coccus is the causative factor in beriberi. The author, working in the Hiroshima Kakke Hospital under the direction of Surgeon-Major Kokubo, has had an opportunity to isolate these identical organisms from cases of beriberi in Hiroshima. A study of the cultures so obtained, as well as of those isolated by Kokubo and Okata, has, however, by no means convinced him of the specificity of these organisms. The author[1] has besides failed to obtain the same coccus from typical cases of beriberi in the Philippine Islands, and inoculation experiments on monkeys with the *Kokubo-Okata kakke coccus* have been absolutely negative. In about fifty cases of beriberi occurring in Manila, cultural examinations by withdrawal of the blood from the cephalic vein, incubating it with bouillon both aërobically and anaërobically, have likewise failed to demonstrate any specific beriberi microbe. Koch, who had previously examined the blood of beriberi patients by this method, likewise had negative results. In spite of the failures to isolate in beriberi a specific organism as the cause of the disease, the evidence is decidedly in favor of the view expressed by Scheube, Baelz, K. Miura, and others, that beriberi is an infectious malady. It has been frequently observed that the importation of a single case or of a few cases of this disease into a territory heretofore free from it has been followed by an extensive general outbreak, though the environmental conditions, the food supply, the nutrition of the population, etc., had not undergone any changes.

Larger outbreaks of beriberi are generally observed where there is a crowding together of many individuals into a limited space, as in prisons, barracks, asylums, schools, vessels, etc. Hence, beriberi frequently has the character of an institutional disease. The climatic conditions most favorable to the development of the disease are moisture and heat. It is most prevalent, as stated above, in tropical and subtropical countries. However, there is one marked exception to this rule, in that it occurs quite frequently in Yezo or Hokkaido, the northernmost island of Japan, in which the climate is somewhat similar to that of the northern part of the United States, Canada or northern Europe. In Japan beriberi is most common in the months of July and August and large epidemics have been noticed particularly during or shortly before these months, when the rainfall has been unusually heavy. In the Philippine Islands it likewise occurs most frequently during the hotter months of the year and during the height of the rainy season. In countries where beriberi occurs, it is usually found in the lowlands near the sea or in alluvial territories along great rivers. It is, as a rule, not found in the higher altitudes, although occasionally it does gain a foothold in mountainous regions. The disease is much more common in the male than in the female

[1] *The Philippine Journal of Science*, vol. i, No. 2, 1906; "Studies in Beriberi," *Ibid.*, No. 7, 1906.

sex. However, attention should be called to the fact that pregnant women seem to be particularly liable to acquire it.

It most commonly occurs between the ages of fifteen and thirty years. It is generally very rare in infancy and early childhood, except in the case of infants fed by mothers sick with beriberi. There is certainly no doubt that some races, such as the Japanese, the Chinese, and the Malay, are particularly prone to contract the disease. Americans and Europeans are generally not very susceptible even when living among the natives where the disease is prevalent. However, their immunity is by no means absolute. The author has seen a few cases of beriberi among Americans in the Philippine Islands, some of which terminated fatally. While beriberi frequently attacks strong, well-nourished young men, it is, on the other hand, also commonly met with as a complication in some chronic wasting diseases. Among these may be mentioned particularly tuberculosis and amœbic dysentery. In many fatal cases of beriberi occurring in Bilibid prison, the great penitentiary of the Philippine Islands, a complicating tuberculosis or dysentery has been found at autopsy.

**Special Pathology.**—In bodies of patients dead of beriberi marked postmortem rigor generally promptly develops. However, in cases which succumb slowly to the atrophic type or in which complicating wasting diseases, such as tuberculosis, amœbic dysentery, etc., are present, the postmortem rigidity may be quite insignificant; this, however, is the exception and not the rule. When death has occurred very rapidly, as in th acute pernicious variety, the author has observed the postmortem rigor develop very early and become as strong as that met with in fulminating cases of Asiatic cholera or bubonic plague. The skin is pale, with yanotic patches here and there. Occasionally cutaneous hemorrhages may be observed.

On section, the superficial veins discharge a large amount of dark fluid blood, and in the majority of cases, excepting only those of the atrophic form of long standing, the subcutaneous tissue is œdematous. The subcutaneous œdema is usually best marked in the anterior thoracic region and over the anterior surfaces of th lower extremities. Hydropericardium, ascites and hydrothorax are very frequently encountered, hydropericardium being the most common. The average among 256 ollected cases show 66 per cent. of hydropericardium. The author has likewis found hydropericardium in the majority of his autopsies. Subepicardial and subpleural petechiæ are also not infrequently encountered. Of the internal organs, the heart shows characteristic changes most constantly. Th myocardium, as a whole, is hypertrophied; this is usually most marked in the right ventricle, but the left may likewise be enlarged. The organ then is increased in all its diameters and in its weight. The average weight in 93 cases reported by Yamagiwa was 368 grams, while that of the normal Japanese heart is from 250 to 300 grams. The right ventricle was hypertrophied in 73 of these 93 cases, the average diameter being 6.1 mm., compared with a normal diameter of 2 to 3 mm. The right ventricle in particular is generally not only hypertrophied but also markedly dilated, so that a relative insufficiency of the tricuspid valve is present. All of the chambers generally contain a large amount of dark fluid blood. The coronary veins are much dilated. The myocardium may be normal, but quite frequently it is found to be more or less cloudy and mottled in consequence of diffuse fatty degeneration. The lungs are, as a rule, œdematous, congested and contain little air;

however, occasionally they are emphysematous, and sometimes collapsed and dry. Occasionally some catarrhal bronchitis is seen, and, when the pneumogastric has been profoundly affected, aspiration pneumonia has been observed.

The spleen shows no changes characteristic of the disease. In the tropics considerable enlargement has frequently been observed but this must be looked upon as a mere coincidence, because in tropical postmortem material, no matter what the immediate cause of death has been, enlargement of the spleen is very frequently found. However, this organ frequently shows cyanotic induration of a moderate degree. The kidneys in acute cases are markedly congested, and moderate cloudy swelling and fatty degeneration are occasionally observed. The liver is generally somewhat swollen and congested. Where chronic passive congestion has existed for some time, there is the characteristic appearance of the nutmeg liver. In many cases, particularly of the subacute variety, which have not existed for a very long period, we find great hyperæmia of the gastric and duodenal mucosa and occasionally ecchymoses. In some cases blood clots are present in the stomach, possibly due to persistent vomiting prior to death. This condition of the gastric and duodenal mucosa has so impressed several observers that they maintain the stomach and duodenum to be the portal of entrance of the specific virus of beriberi. The writer, like others, has observed this hyperæmia in the majority of autopsies, but is inclined to look upon it as a purely mechanical "Stauungshyperämie," due to general venous congestion, which often finds so marked an expression in the liver. The small intestine, excepting the duodenum, and the large intestine show no particular changes.

The peripheral nerves, particularly those of the lower extremities, are almost without exception profoundly affected but the changes are rarely noticeable to the naked eye. The lesions found on microscopic examination clearly indicate that the most characteristic anatomical morbid process is the degeneration of the peripheral nerves. This observation was first made by Baelz, Scheube, Miura and Yamagiwa, and has been confirmed by many other observers. The microscopic changes are a degeneration of the myelin sheath and of the axis cylinder. The former breaks up into roundish or irregular fragments, which are arranged more or less like a row of beads. Later the myelin sheath may also show a honeycombed or foamy condition, or it may disappear entirely over longer distances of the nerve fiber. When such is the case, the axis cylinder likewise gives evidence of degeneration. It is irregularly twisted and retracted and finally also entirely disappears so that nothing is left but an empty collapsed neurilemma. The nuclei of the latter are increased, but there is nowhere any sign of an active inflammatory process, although there may be a moderate number of leukocytes, evidently phagocytes, which enclose material from the degenerating myelin substance. The muscles supplied by such nerves likewise show degenerative processes. These manifest themselves first by a loss of striation. Where the process is more advanced, the sarcoplasm is changed into irregular hyaline masses; the fiber, as a whole, is shrunken, and between these masses clefts and spaces are seen, which, during life, were filled with an œdematous exudate.

Yamagiwa,[1] from a large autopsy material, enumerates the following as the most important pathological changes: (1) Dilatation and hypertrophy

[1] Yamagiwa: "Beitrage zur Kenntniss der Kakke," *Vir. Arch.*, 1899, clvi, p. 451.

of the right ventricle, and dilatation of the left; fatty metamorphosis of the myocardium; (2) degeneration of the peripheral nerves; (3) atrophy and degeneration of the skeletal muscles; (4) parenchymatous degeneration of the kidneys; (5) hydrops. In other words, all the pathological changes are regressive in nature, with the single exception of the hypertrophy of the myocardium.

**Varieties and Symptoms.**—From a clinical standpoint, beriberi may be divided into three chief forms, namely, acute pernicious, wet or œdematous, and dry or atrophic beriberi. This classification is, however, somewhat arbitrary. Besides the three well-defined forms, a rudimentary variety occurs quite frequently, in which the symptoms are so mild that medical aid is generally not sought. In these cases there is generally noticed a certain malaise, weakness of the lower extremities, and increased heart beat on slight exertion. These symptoms may speedily disappear spontaneously, or increase in intensity and lead to one of the severer forms of the disease.

FIG. 2.

Wet beriberi, showing œdema of the legs and feet. (Author.)

In the acute pernicious form, the onset is generally quite rapid. The patient becomes ill, apparently without premonitory symptoms. A feeling of oppression develops in the chest, dyspnœa, forced respiration, evidences of great venous congestion, frequently vomiting and the signs of rapid heart failure appear and death supervenes. Both the œdematous and the atrophic types generally develop in the same manner. Preceding the actual outbreak, there is a period of malaise, during which dull pain in the stomach, lack of appetite, and heaviness in the lower extremities and occasionally in the upper ones are complained of. One of the earliest symptoms usually referred to by the patient is palpitation of the heart on slight exertion; next, pain in the legs is frequently noticed, particularly in the calves, which soon become tender on pressure. Later the gait becomes unsteady; the patient walks as if it were difficult, as indeed it is, to lift the feet from the ground. The gait of a person sick with beriberi has not been improperly compared to that of a man walking in soft and very sticky clay, or to that of a man, heavily dressed, who has been in the water and whose clothing is heavy from the fluid absorbed. At this stage, in the case of the *wet* form, an œdema of the lower extremities is generally noticeable. It is particularly well marked over the anterior tibial region, over the dorsum of the feet and around the ankles. Here the skin pits on pressure. In the *dry*

form, a slight œdema may be present at an early period, but this is not well marked and is transitory. The lower extremities in this variety, instead of being swollen, progressively become more and more emaciated and the muscles become atrophic, often indurated and contracted. Together with the disturbances of locomotion, disturbances of sensation develop simultaneously.

Hypæsthesia of the lower extremities is the most common form of disturbance of sensation. This generally begins on the anterior or external surface of the legs and frequently extends to the dorsum of the feet and toes. It is found in the territory supplied by the peroneal and saphenous nerves. Accompanying hypæsthesia, there is a subjective paræsthesia. If the skin is touched with a soft camel's hair brush, the patient feels as if paper intervened between the skin and the brush. The intensity and the extent of such disturbances of sensation vary not only in different individuals but also at different times in the same individual. These disturbances have a tendency to spread upward from the feet and legs. In the severer cases the upper extremities are similarly affected. The face is rarely involved, but occasionally disturbances of sensation are found around the mouth. True anæsthesia is rare, as is also hyperæsthesia. The disturbances of motility generally begin as a sensation of weakness in the legs, which is first noticed in the calves and later on in the thighs. After these have lasted for some time, atrophy is generally evident or it may appear even before distinct paralysis becomes obvious. Usually the anterior sharp edge of the tibia becomes more prominent, the calf becomes thin and flabby and the thigh

FIG. 3.

Dry beriberi with great atrophy of the muscles of the legs and equinovarus position of the feet. (Author.)

gradually becomes emaciated. When more or less contraction is associated with the atrophy, the foot assumes an equinovarus position. In severe attacks, similar changes occur in the upper extremities. Paralysis of the lower extremities is much more common than paralysis of the upper ones; but in the severest cases both feet and hands, including the toes and fingers, may be paralyzed. The hands and fingers in such cases may occasionally be more affected than the feet. In the gravest types neither the hands nor the fingers can be flexed toward the dorsum, and there is complete wrist-drop.

The electrical excitability shows various degrees of change, from a simple diminution to a complete reaction of degeneration. According to K. Miura, one can foretell from the position of the foot and toes the result of the electrical tests. If the foot can be moved easily on the ankle-joint, one finds only a diminution of electrical excitability. If the toes, but not the foot, can

be flexed dorsally, we encounter only a partial degeneration reaction. If, however, neither the foot nor the toes can be moved voluntarily, we then have a complete degeneration reaction. Paralysis of the diaphragm and of the intercostal muscles occurs only in the severest cases. In addition to the nerves of the extremities, other nerves are also more or less frequently involved. Paresis of the muscles of the larynx is by no means rare; in fact, it is a very common occurrence to find hoarseness and more or less complete aphonia. Paresis of the facial nerves and of the nervus abducens has occasionally been observed, as also have been disturbances of the optic nerves, manifested by central scotoma, and in rare cases by amblyopia. Among the late symptoms, which at this time become frequently quite prominent, are contractions of the muscles, particularly of the gastrocnemius.

If an early examination be made, both in the hypertrophic form and in the atrophic dry one, the following symptomatology may be found; the pulse is generally rapid, somewhat irregular, rather weak and easily compressible. On slight exertion, sometimes even so slight as sitting up in bed, the rate increases 20 or 30 beats a minute. The apex of the heart, sometimes quite early and frequently later after the disease has existed for several days, is found displaced upwardly and outwardly and the area of visible impulse is enlarged. The area of heart dulness is increased to the right. Where there is hypertrophy of the left ventricle, the area of dulness is also increased to the left. At the apex some change in the first sound may be found; but the most common sign is generally a marked accentuation of the second pulmonic sound. Sometimes a definite systolic bruit may be heard at the apex. Frequently there is a reduplication of the second sound both at the apex and in the pulmonic area. In a considerable number as was first prominently pointed out by M. Miura, a musical sound is heard over the crural arteries, which may be audible even at a distance of several feet from the patient.

In the early stages, sometimes up to the sixth or seventh day, the patellar reflex is increased. Then a diminution of the knee-jerks appears, and finally they are entirely absent. Even in cases which terminate favorably the absence of the knee-jerk may last a long time and may be present after the disturbances of locomotion have disappeared. When the knee-jerk begins to reappear, it generally again becomes temporarily accentuated, and then finally returns to the normal. It has already been mentioned that the muscles of the calves of the leg are frequently painful and very tender to pressure. The skin, particularly of the lower extremities, shows disturbances of sensation. There is general hypæsthesia or paræsthesia, and less frequently complete anæsthesia.

In mild cases the urine is somewhat decreased in amount, and in severe ones considerably so. The diminution is sometimes very great, and the daily amount may fall below 100 cc. The specific gravity in such cases is increased, but not proportionately to the great diminution in amount. Albumin is generally not found. When, however, it is present, only traces occur. However sometimes, though rarely, a complicating nephritis develops in the later stages, and then albumin is constantly present. Indican is very frequently found in the acute and œdematous varieties.

According to most authors, the temperature in uncomplicated cases is either normal or very slightly elevated. When a marked rise of temperature is met with, it is usually owing to some complication. In all cases seen by the

writer in which there was a marked rise in temperature during life, at autopsy some complicating lesion was found.

In cases either of the œdematous or the atrophic form which progress unfavorably, the dyspnœa and the difficult respirations increase and the resulting grave circulatory disturbances find their expression in a superficial venous congestion, with visible throbbing veins. While consciousness is preserved, the dyspnœa and the suffering increase, and the face of the patient presents a picture f grave anxiety, such as may be seen in angina pectoris. Death frequently occurs quickly in consequence of heart failure. Stanley[1] has drawn attention to the frequency of *sudden heart failure* in diphtheria and in beriberi. His analysis of 340 cases of the latter disease shows 72 fatal instances, of which 31 died of rapid heart failure. The pulse tension was lowered in 254 cases, and dilatation of the heart existed in 98. The second sound was reduplicated in 245, and the first in 35. There were cardiac murmurs in 84. When the disease ends in recovery, the disturbances of circulation decrease in intensity. In the wet form there occurs a profuse secretion of urine and the œdema gradually disappears. In both types which progress favorably, the disturbances of sensation and the paralysis disappear gradually and the patient regains the use of his limbs.

Beriberi occurring in infants fed by mothers sick with the disease has been described by Hirota. In these the disease generally presents the symptoms of the acute pernicious type, namely, restlessness, vomiting, dyspnœa, aphonia, rapid pulse, extension of the heart dulness toward the right, œdema, a musical sound over the crural artery, and absence of fever. When the child is taken away from the sick mother early, the symptoms generally disappear within two weeks.

**Complications and Sequelæ.**—The most common diseases associated with beriberi are tuberculosis and dysentery. When these co-exist the prognosis is usually very grave. While most cases of beriberi end in rapid recovery, some have a protracted course and general weakness with or without anæmia, difficulty in the use of the lower extremities, contraction and induration of the muscles of the calf, and also disturbances of motility in the upper extremities with diminution and disturbance in the quality of the sensation; palpitation of the heart and rapid pulse may remain for a long time. As a rule, these symptoms all disappear under proper treatment and diet. It has been noticed in Europeans or Americans who have suffered from severe attacks of beriberi and who have returned during convalescence to their native country, that the disease assumes generally a protracted course from which recovery is very slow.

**Diagnosis.**—In many cases among the uneducated and ignorant Asiatics, the diagnosis must be made exclusively from the objective symptoms, as an intelligible history is unobtainable. The most important points are the condition of the pulse while the patient is at rest and before he has been disturbed, and after he has been subjected to some physical exertion. If the patient is not too ill, he should be made to leave his bed and walk up and down the room a few times. While doing so the gait should be noted in order to ascertain whether it presents the characteristic appearance already mentioned. The pulse is then again to be counted. In beriberi it is usually accelerated and the rapidity increases very mark-

[1] *British Medical Journal*, December 26, 1903.

edly on slight exertion. The percussion and auscultation of the heart are also of value. Particular importance attaches to the enlargement of the right ventricle, to the accentuation of the second pulmonic sound and to a reduplication of the second sound. The frequency of hydropericardium, hydrothorax and ascites are valuable points, as also the increase of the patellar reflex in the early stages and the loss of it in the more advanced ones. The frequency of pain in the muscles of the calf, and of œdema in the leg and foot, have already been noted. The great decrease or even the suppression of the urine in the early stages of the œdematous form is also an important factor. The disturbances of sensation and of locomotion and the paralyses and contractions have already been emphasized.

Among the diseases which might be confounded with beriberi are the following: *Myelitis* in which are present increased reflexes, ankle clonus, paralysis of the extremities without muscular atrophy, paralysis of the bladder and rectum, complete anæsthesia without pain in the muscles of the calf, no reaction of degeneration and no symptoms on the part of the heart and kidneys. In *Landry's paralysis* there is fever at the onset, and pain in the head, with much perspiration at the back and extremities. A study of the sensation and circulation reveals nothing abnormal. *Tabes* should not be confounded with beriberi or *vice versa*. In *anæsthetic leprosy* a thickening of the peripheral nerves and a true anæsthesia is found and not hypæsthesia, which is generally encountered in beriberi. In addition, in leprosy, spots or nodules or diffuse thickening of the skin are usually encountered. A careful search will reveal the presence of the lepra bacillus. Certain cases of *peripheral neuritis*, depending upon chronic alcohol or arsenic intoxication, may at times be exceedingly difficult to differentiate from beriberi. In Europeans and Americans living in tropical countries where beriberi is prevalent, and presenting symptoms suggesting the possibility of an attack of this disease, *alcoholic neuritis* should first be excluded definitely before a diagnosis of beriberi is made. In Japan, and in the Philippine Islands, where beriberi is so prevalent and so well known, patients frequently consult the physician with the simple statement that they are suffering with this disease. But, of course, such a statement cannot be accepted without verifying its correctness by a proper examination.

**Prognosis.**—The prognosis varies greatly in different epidemics and in different localities. It is perhaps most fatal (an observation commonly made as to infectious diseases) when it first invades a new territory in which it has never been prevalent before. A very interesting account of what appears to have been the first outbreak of beriberi in the Philippine Islands has been published by Koeniger.[1] This author reports that when the disease first broke out in Manila, in October, 1882, its victims succumbed without exception and that the mortality during the first few months was not less than 60 per cent. Among Chinese in Sumatra and Java, epidemics with an equally high mortality have been observed. Stanley gives a mortality of 20 per cent. among the Chinese prisoners at Shanghai. Among the Chinese patients of the Hong Kong government hospitals during the last ten years, the mortality has been 50 per cent.[2] The death-rate in cases developing in

[1] *Deut. Arch. f. klin. Med.*, 1884, xxxv, p. 419.

[2] Personal communication from Dr. M. V. Koch, Physician in charge of the Government Civil Hospital for Infectious Diseases.

Bilibid prison at Manila is likewise quite high.[1] These instances, however, represent somewhat exceptional and particularly unfavorable conditions. Under favorable conditions, the mortality is usually low. In Dutch India among the troops, the death-rate is given as between 2 and 6 per cent. Among the English East Indian troops the figures are somewhat higher. Scheube gives an average mortality of 3.5 per cent. for Japan. During the first year (1904) of the late Russo-Japanese war there were sent back from the front to the Military Reserve Hospitals of Hiroshima, Tokyo, etc., 50,340 Japanese soldiers sick with beriberi. Of these, 1,024, or less than 2 per cent., died. During the same period of time there developed among the troops in Japan 3,337 cases, of which only 44 died. So, on the whole, taking a very large material as a basis, the prognosis is quite favorable.

No definite prognosis can be made in an individual case, because a fatal termination from heart failure may occur at almost any stage during the course. Unfavorable symptoms are marked dilatation of the heart, great weakness and irregularity of the pulse and other grave disturbances of circulation, circumscribed œdema on the trunk, signs of œdema in the lungs, and particularly persistant vomiting. The last symptom is almost invariably the precursor of a rapid fatal termination in consequence of heart failure. The mortality in the acute pernicious form is always high; that in the subacute or chronic, œdematous type is lower but higher than in the dry atrophic variety. A favorable sign is the appearance of a copious renal secretion after partial or complete suppression of urine. Acute pernicious cases when fatal always terminate by heart failure or asphyxia; in chronic cases death results from paralysis of the respiratory muscles, occasionally from aspiration pneumonia or by general debility. The latter event is particularly liable to take place when tuberculosis or amœbic dysentery is present. The average duration of acute pernicious beriberi is very short, while that of cases of moderate intensity and of moderately chronic character is perhaps between three and six weeks. Besides these there are a large number of protracted cases, which extend over a period of months and sometimes may last more than a year. These very chronic cases are characterized by muscular atrophies and joint fixations. But generally even these patients, if properly treated, and if placed under proper hygienic conditions, proper nutrition, etc., finally become completely well.

It has been, however, frequently noticed in Japan, the Malay Peninsula and the Philippine Islands, that if a patient has had one attack, although he recovers completely, when exposed to the same conditions which brought on the first attack, he suffers a second or even a third one. In this respect beriberi may be likened to diphtheria and some other infectious diseases, an attack of which in certain individuals leaves a predisposition to subsequent ones.

**Prophylaxis.**—This is still in a decidedly unsatisfactory state. The observance of the ordinary rules of hygiene and sanitation has frequently shown a favorable influence in restricting the disease. However, in other instances, beriberi will become prevalent in certain localities and under certain conditions, in spite of all hygienic and sanitary measures. The late Russo-Japanese war furnishes a confirmatory example of this statement. The hygienic measures adopted in the Japanese army proved sufficient to limit to a minimum such diseases as typhoid, typhus, dysentery, scorbutus,

[1] Bilibid prison in Manila contains from 3,500 to 4,500 prisoners and the hygienic conditions, under the circumstances, formerly were necessarily not the very best.

etc., but they were of no avail against beriberi. There is one factor which beyond all doubt favors the occurrence and spreading of beriberi in those countries and among those races where it is at all prevalent, that is, the crowding together of large numbers of persons into limited spaces, as prisons, barracks, schools, factories, mines and ships. If beriberi appears under such environments, these places should, if possible, be abandoned as dwellings, at least, the number of inmates should be decreased, and a thorough disinfection, airing and drying should be undertaken. The statements as to the effects of a change from a rice diet to some other, as a prophylactic against beriberi, are up to the present time so hopelessly contradictory that reliable conclusions cannot be drawn from them. Women sick with beriberi should not nurse children.

**Treatment.**—There is no specific treatment. The patient should be confined to bed. Even if he is suffering from what appears to be only a mild attack, nevertheless rest, in the beginning, should be insisted upon, since it is important to reduce the heart's action as much as possible in order to guard against future and often unexpected grave cardiac complications. It has generally been found very advantageous to administer the saline laxatives in large doses during the first stages of beriberi. A favorite Japanese prescription is the following:

℞ Magnesii sulphatis.....30 to 50 grams.
Acidi muriatici diluti.....1.5 to 2.0 cc.
Tincturæ amaræ.....4.0 cc.
Aq. q. s. ad.....200.0 cc.
30 cc. (1 ounce) three times a day.

This is to be given for from five to seven days, followed by an intermission of a few days, after which the treatment is repeated. Other drugs recommended are cream of tartar, infusion of senna, Carlsbad salts, oleum ricini and aloes and jalap in the form of pills. Where there is marked œdema, Baelz and K. Miura recommend potassium acetate (90 gr., 6 gm.), potassium nitrate (30 gr., 2 gm.), or diuretin (45 to 60 gr., 3 to 4 gm., per day). Scheube has strongly recommended the use of digitalis, but most observers consider it of very doubtful value, and it has been repeatedly stated that in many cases it has a decidedly injurious effect in that it tends to produce anorexia, nausea and vomiting. In severe acute cases with great weakness of the heart, Baelz frequently observed good effects from large doses of cocaine given internally in amounts of from 1 to 3 grains (0.05 to 0.20 gm.) per day. In acute or subacute cases, with signs of dilatation of the right heart, while the pulse is still good, encouraging results have been obtained by bleeding, to the amount of several hundred cubic centimeters. However, when the pulse has become weak, this is dangerous, on account of the possibility of sudden heart failure. With dilatation, venous congestion and a weakened pulse, the withdrawal of blood by cups or leeches, applied over the precordial region, is often followed by improvement. The author has seen a considerable number of Japanese soldiers sick with beriberi who were greatly helped by this. However, the improvement is frequently only temporary and a repetition of the procedure may or may not bring about good results, or the unfavorable symptoms may increase in severity in spite of a temporary amelioration.

The *diet* should be light and nutritious and include considerable milk. Both in Japan and in Java beriberi patients frequently receive as a part of

their daily nourishment the Adzucki bean (*Phaseolus radiatus*), which, it is believed, has both a favorable prophylactic and a curative tendency. In the Philippines similar virtues are claimed for the Mongo or Mungo bean (*Phaseolus Mungo L.*). Rice should, in private practice at least, be withdrawn from the diet. This measure is necessary, not so much on account of its real value, as on account of the fact that there is still a widespread popular belief, in many regions where beriberi prevails, that a kakke patient should not eat rice. Hence, a physician who fails to remove rice from the daily dietary is liable at once to lose the confidence of his patient. A person sick with a severe type of beriberi, accompanied by grave circulatory disturbances, should not under ordinary conditions be moved to a distance. Even during the early stages of recovery, a long railroad journey may bring on a relapse with severe and dangerous heart symptoms. But cases mild from the onset, and serious ones after recovery, may with advantage be removed from a beriberi-infected neighborhood to a high and dry locality free from this disease. If there is a marked hyperæsthesia (which, however, is rare in beriberi), bromide of potassium or morphia internally or chloroform externally are recommended. Vomiting and dyspnœa are frequently greatly ameliorated by the hypodermic administration of small doses of morphia.

It is very important that the muscular atrophies and contractions should receive early and proper treatment. However, it is not advisable to begin this as long as there is marked œdema of the affected extremities. When the œdema has subsided, massage and passive movement are to be practiced systematically several times a day. As soon as the patient is able to do so, and when there is no longer any immediate danger of cardiac failure, moderate active exercise should be cautiously begun. Should such exercise lead to a very marked increase in the pulse rate, it should be postponed. The atrophic muscles are to receive electrical treatment. When they still react to the faradic current, the latter is to be used. Where there is complete degeneration reaction, the galvanic current should be employed, with the cathode situated peripherally over the nerve and the anode centrally applied. In the use of the faradic current, Scheube recommends large sponge or roller electrodes, to be employed in a massaging manner. When there is paralysis of the phrenic nerve, M. Miura advises faradization, one sponge electrode being placed over the epigastric region and the other above and inside of the sternoclavicular articulation, or the two electrodes may both be placed on the sides of the neck.

For Europeans and Americans who have suffered from an attack of beriberi, a change of climate and return to a more bracing atmosphere should be recommended.

# CHAPTER III.

## ANTHRAX. RABIES. GLANDERS.

By MAZŸCK P. RAVENEL, M. D.

### ANTHRAX.

**Synonyms.**—English, splenic fever; wool-sorters' disease; malignant pustule; anthracæmia; French, charbon; sang-de-rate; mal-de-rate; fièvre charbonneuse; charbon bactéridien; anthrax; German, Milzbrand.

**Definition.**—Anthrax is a specific and highly contagious disease common to man and most domestic animals, due to the *Bacillus anthracis*. It occurs in two principal forms: an external, due to direct inoculation through a cut or abrasion; and an internal, caused by ingestion or inhalation of the spores or bacilli.

**Historical.**—Anthrax has been known in man and animals for many centuries, and, although a number of inflammatory diseases have been described under the name, the descriptions of certain plagues given by ancient authors are sufficiently exact to enable us to recognize what we now know as anthrax. The sixth plague of Egypt is believed to have been anthrax by some authors. It was not until the latter part of the sixteenth century that contagion from animals to man was suspected, and only during the latter half of the eighteenth century that order began to come out of chaos, chiefly through the efforts of Chabert (1780), who first differentiated the disease from the inflammatory and gangrenous affections with which it was universally confounded and gave a classification which is employed almost in its entirety at the present day. He recognized three forms: (1) Charbonous fever,—internal anthrax, without external lesion; (2) essential charbon, marked by a primary external lesion,—malignant pustule; (3) symptomatic anthrax, in which there is primary fever, with secondary appearance of tumors. The third form is now known to be a separate disease (black-quarter; rauschbrand), confined almost exclusively to cattle and not communicable to man. The contagiousness of anthrax was first experimentally proven in 1823, by Barthélemy, who infected animals with the blood both by inoculation and ingestion.

The discovery of the bacillus by Rayer and Davaine[1] was made in 1850, who observed in the blood of animals with anthrax "little filiform bodies, in length about twice the diameter of a red corpuscle, and without movement." They did not recognize the significance of their discovery. In 1855, Pollender announced that in 1849 he had observed the bodies seen by Rayer and Davaine. He recognized their vegetable nature, but did not attribute any importance to them. Brauell, in 1857, observed the rods in the cadaver, and also just before death. He attributed to them a diagnostic and

[1] *Comptes Rendus Soc. Biol.*, 1850.

prognostic value but did not suspect their causative relation to the disease. In 1860, Delafond cultivated the bacilli by putting anthrax blood in glass flasks. He foresaw the formation of spores but was unable to demonstrate them, nor was he sure whether or not the rods were the effect or the cause of the disease. Pasteur's work on butyric acid fermentation, in 1859, gave new light to Davaine, and he once more took up the study of anthrax, in the belief that the rods he had discovered were the cause of the disease. He showed that they were constant in the blood of anthrax, and that, when filtered, such blood could be inoculated without harm into other animals.

The bacillus was cultivated on artificial media in 1876 by Koch, who discovered the spores and proved its etiological relation to the disease. In 1877, Pasteur confirmed the work already done and greatly extended our knowledge of the biology and pathogenesis of the organism.

**Anthrax in Animals.**—Since anthrax in man is always derived from animals either directly or indirectly, its distribution is a matter of importance. Known from the earliest times, it remains to-day one of the most widespread and destructive of animal plagues. It is found in practically every part of the world, but is especially prevalent in parts of France, Germany, Austria, Italy, Turkey, Russia, China, South Africa, and South America. Considerable losses occur in the United States from time to time, in widely separated parts of the country. In countries where it is endemic it is especially active during certain years.

The herbivorous animals are particularly affected. In Russia, large numbers of horses perish from the disease, and their hair, which is largely used in manufactures, is responsible for the infection of man in distant portions of the world. The most dangerous hair comes from China, Russia and Siberia. In Asia Minor, anthrax is prevalent among the Angora goats, which supply much of the mohair of commerce, the source of many of the cases of wool-sorters' disease.

Anthrax does not spread from animal to animal by contact or association, infection taking place as a rule, through the intestine, from the ingestion of forage ntaining the spores. The refuse from tanneries and the washings from infected wools have been proven to play an important part in the spread of anthrax, through the infection of pastures. A striking instance of infection from tanneries occurred in Pennsylvania, where, almost simultaneously, anthrax appeared among the operatives of three tanneries quite widely separated, and in the cattle pastured on the streams which received their drainage. The source of infection proved to be a cargo of hides from China which had been divided among the three plants. Russell has reported a similar case in Wisconsin, the tannery using hides from South America and China. In Delaware, the morocco works using goat skins from South America are a frequent source of infection for native cattle. Houston has found anthrax bacilli in the mud of the river Yeo at Yeovil in England.

The dust from factories working up infected materials may also spread the disease, as in the case reported by Silberschmidt at Zurich, where 8 out of 22 horses were infected by grazing in a lot exposed to the dust from a horse-hair factory.

A field once infected is difficult to rid of anthrax. Pasteur showed that the spores from soil infected by the blood and corpses of animals which had died of anthrax were brought to the surface by earthworms. Fields are also infected by the use of waste products from tanneries and factories as fertilizer.

In lessening the ravages of anthrax, Pasteur's method of vaccination has played an important part, and should be practised in horses, sheep, cattle, etc., whenever exposed. Unfortunately the immunity produced is not lasting, but usually one vaccination a year is found sufficient. Infected premises must be cleansed and disinfected, and cattle from infected herds should not be carried into new districts. Most important is the destruction of the carcasses of dead animals. Whenever possible they should be burned. Failing this, they must be deeply buried and covered with quick-lime. Under no circumstances should the skin be removed nor the body opened, as this admits oxygen and allows the formation of spores. In the absence of spores the anthrax bacillus is rapidly destroyed during putrefaction.

**Etiology.**—The study of anthrax has a special interest, inasmuch as it was the first disease in which the etiological relation between a bacillus and a disease was ever shown. Much of our general knowledge of the nature of bacteria has been gained from the study of the anthrax bacillus, and it has also gone far to establish the germ theory of disease.

Anthrax in man is always derived from some domestic animal, or from some commercial animal product, especially the hide, hair, or wool. The bacillus does not penetrate the unbroken skin, but enters some abrasion, scratch, or cut.

In the United States it occurs almost exclusively among veterinarians, brush makers, leather workers, and tanners. Farmers are sometimes inoculated while skinning animals which have died of anthrax, and butchers from handling the meat of diseased cattle. Among others who are especially exposed to contagion are knackers, plasterers, felt makers, and mattress makers. Internal anthrax is almost unknown in this country. It is quite common in certain portions of England, notably the Bradford district, where wool and hair from many parts of the world are manufactured, and which receives almost the total importation of what are known as dangerous wools. Much of our knowledge of this type of the disease has come from the very excellent studies made in this district, where it has received the name "wool-sorters' disease."

It was first observed after the introduction of alpaca and mohair, in 1837. Outbreaks occurred from time to time, which were studied by eminent physicians, but the etiology was not definitely demonstrated until 1880, when Mr. Spear and Professor Greenfield made an exhaustive investigation at the instance of the Local Government Board, although in 1879, Bell had successfully inoculated animals with the blood of an alpaca sorter shortly before death, and recovered anthrax bacilli from their blood, being the first to recognize the disease as anthrax.

Infection takes place usually in the sorting, combing, and spinning of the wool, and is due to the inhalation of the spores of anthrax which are given off in the dust arising from the wool of diseased animals during these operations. Other things being equal, the danger from wool and hair is inversely proportioned to their moisture or greasiness, which prevent the spore-containing dust from flying off. Cutaneous inoculation takes place from greasy wools, but never the internal form. Wools from hot climates are often dry and dangerous. The hair of goats, cows, horses, alpacas, etc., does not contain any greasy matter, and is especially dangerous. Even where goats and sheep are herded together and thus exposed in the same degree to anthrax, the wool will be comparatively safe to work with, while the hair

from goats equally contaminated will be dangerous. The comparative danger from various materials is illustrated by the statistics gathered in England for the six years, 1899 to 1904 inclusive, during which time 261 cases of all forms of anthrax were reported with 67 deaths, as follows:

| | |
|---|---|
| Workers in worsted and wool | 88 |
| Workers in horse-hair and bristles | 70 |
| Workers in hides and skins | 86 |
| Workers in other industries | 17 |

Workers in hides and skins acquire almost exclusively external anthrax. In London, of 92 cases observed among those working in the hide and skin trades, only 2 were intestinal, while of 87 cases in the Bradford worsted districts, 30 were external and 57 internal in form.

The very fatal disease observed in rag pickers in the paper mills in lower Austria (*Hadernkrankheit*) has been shown by Frisch and Eppinger to be internal anthrax.

Gastro-intestinal anthrax may result from eating the flesh or drinking the milk of animals with the disease. Fortunately, the disease is so rapid in its course that danger from these sources is not very great. The writer has known an animal in the last stages of anthrax to be slaughtered and dressed for market by a thrifty farmer who saw his cow about to die, and wished to avoid loss. Examination of the blood of this animal proved it to be swarming with anthrax bacilli.

Billings states that in the Bavarian Alps it is common for the farmers to conceal the presence of anthrax in their cattle and to dress the diseased animals for food, preserving the flesh in pickle. As spores do not form during life, nor after death unless the supply of oxygen is abundant, such flesh will contain vegetative bacilli for the most part, if not entirely, and these are readily destroyed in cooking.

External anthrax can unquestionably be conveyed by flies and other insects, though this is probably a rare method of infection.

**Sex.**—The victims of anthrax are almost always men, since women are not often employed in the callings which expose one to infection.

**Bacteriology.**—The bacillus of anthrax is one of the largest of the pathogenic bacteria. The individual rods are 1.2$\mu$ thick and 6 to 8$\mu$ long. The ends are characteristic, being square-cut or even depressed, so that in chains the elements are separated by a lens-shaped space. It forms very long filaments in suitable culture media. It stains readily with the usual basic aniline dyes, and is not decolorized by Gram's method. Colonies on agar and gelatine are very characteristic. They are made up of wavy masses like locks of hair, radiating from the centre. The edges of growths on slanted agar present the same appearances. In bouillon, a delicate flocculent growth takes place, resembling bits of Japanese paper, or shreds of cotton suspended in liquid. Later, the growth tends to settle to the bottom. In gelatine stab-cultures the growth is equally characteristic. Radiating from the central puncture are innumerable very delicate spikelets pushing out into the gelatine, sometimes being spirals.

The bacillus grows best at 35° C. and ceases to grow below 12° C. or above 45° C. It owes much of its pathogenic power to its property of forming spores. This takes place best at 32° C. and the presence of oxygen is necessary. These spores are remarkable for their power of resistance to external

agencies such as heat, drying, chemicals, etc., which destroy the vegetative bacillus readily. When dry the spores retain their vitality and virulence indefinitely, and it is through their agency that the disease is transported from distant parts of the world on hides and wool. Székely found the spores in dried cultures alive and fully virulent after eighteen and a half years.

Moist heat of 70° C. kills the bacilli in one minute, but the spores must be subjected to live steam or boiling for more than five minutes and to dry heat of 140° C. for at least three hours to insure their destruction. Cold has no effect on them. The writer has kept them immersed in liquid air at a temperature of 212° F. below zero for three hours without any perceptible effect.

They resist a 5 per cent. solution of carbolic acid always for two or more days, and sometimes for as long as forty days. Corrosive sublimate (1 to 1000) usually kills them in two hours, but Esmarch has found them to resist a 1 to 100 solution for three days, though virulence was lost in twenty hours. The resistance of spores appears to vary somewhat in different cultures, but is always very great. Unlike the vegetative organism, they are unharmed by the action of the gastric juice, and in cattle, where inoculation generally occurs through the digestive tract, are practically always the agents of infection.

The ordinary processes of tanning leather do not affect them injuriously. The writer has kept them immersed for two hundred and forty-four days in the strongest tanning fluids—twice the usual time required in the process—without any perceptible change in their vitality or virulence.

Spores are not found in cultures kept at temperatures below 18° C. nor above 42° C. Grown above 42° C. the bacillus loses the power of forming spores entirely, becomes gradually attenuated, and acquires vaccinal properties. When brought to this condition the attenuated bacillus can be cultivated at ordinary temperatures, without regaining virulence or the spore-forming power. The vaccines of Pasteur are prepared in this manner, the degrees of attenuation depending on the number of days the culture is kept at 42° to 43° C. The first, or weakest, vaccine is grown for about twenty-four days, at the end of which time it has lost the power to kill larger animals, and even guinea-pigs, but will still kill white mice; the second vaccine is grown for about twelve days, and should kill guinea-pigs but not rabbits. In practice, an interval of twelve to fifteen days is allowed to elapse between the two inoculations, which are made subcutaneously.

**Pathogenesis.**—Practically all the domestic animals are susceptible. Fowls are refractory under normal conditions, but can be made susceptible by lowering their temperature. Dogs and cats are sometimes accidentally infected. The herbivora are most susceptible, the carnivora less so, although instances of the disease have been known in lions, tigers, bears, jaguars, etc. Man occupies an intermediate position in the scale of susceptibility.

The action of the anthrax bacillus has been the subject of much discussion, and is not yet thoroughly understood. Attempts to isolate the toxin, by Sydney Martin, Marmier, Hankin and Wesbrook, Conradi and others, have given very contradictory results, and none of them have succeeded in isolating from cultures substances which produce the effects on animals of the living bacillus. Conradi doubts the production of a toxin. There can be little doubt, however, that in the living body the bacillus elaborates bodies which either directly or indirectly are toxic to the tissues. In no other way can the extensive inflammation and œdema be explained. It is perfectly possible that in the body, substances are formed which are not elaborated in cultures.

**Morbid Anatomy.**—Whatever the original port of entry, the postmortem appearances have the same general character, varying according to the duration and the localization of the lesions. The body becomes quickly discolored—in two to four hours,—and decomposition sets in early. The cellular tissues, especially about the neck and chest, become the seat of a putrid emphysema, sometimes with very great distension. From the mouth, nose and other orifices, runs a dark, chocolate-colored fluid. The blood is fluid and almost black in color.

In rapid cases there may be only congestion of the lungs, ecchymotic spots on the pleuræ and pericardium, with a small amount of effusion, the liver and kidneys showing cloudy swelling and enlargement. Sometimes hemorrhages are found in the lungs, heart, kidneys, and other organs. In the majority of cases the lesions are more marked. They consist principally in serous or gelatinous effusions, sometimes blood-stained, into the tissues about the trachea, pharynx, root of the lungs, anterior mediastinum and kidneys. These effusions are frequently seen also in the omentum and mesentery, in the subperitoneal tissues, and sometimes along the retroperitoneal glands. Large serous effusions into the pleuræ and pericardium are common. Less frequently the peritoneal cavity contains fluid. There is great enlargement of the bronchial glands, with ecchymoses and hemorrhages in and about them. Hemorrhages, varying from minute points up to large extravasations, occur in the lungs, mucous membrane of the trachea and bronchi, pericardium, heart muscle, under the capsule of the kidneys, and sometimes in the cortex of the brain, and the pia mater. The heart muscle is dark, soft and flabby. The spleen is sometimes, but not constantly, enlarged, congested and soft. When much enlarged the pulp is almost black and diffluent.

In pulmonary anthrax, Greenfield has made the most complete microscopic studies. He describes the characteristic lesion as occurring in the lower trachea and larger bronchi. The bacilli are found in large numbers in the mucous and submucous tissues, chiefly in the lymphatic vessels, and in the lymphatic plexuses around the arteries. Inflammation takes place, with exudation beneath the epithelium, and later hemorrhage into the substance of the membrane.

In intestinal anthrax the local lesions are found chiefly in the stomach and small intestine. They appear as hemorrhagic areas, somewhat elevated, dark-red in color, and surrounded by an œdematous, injected zone. The centre of the lesion is sometimes ulcerated or gangrenous. Microscopically, the capillaries are found to be dilated, and there is an albuminous exudate rich in leukocytes, or hemorrhagic extravasations. Bacilli are plentiful on the surface of the ulcerations and in the deeper structures.

**Malignant Pustule.**—Studies of the skin lesion were first made by Davaine, and since by Wagner, Koch, Strauss, Cornil and others. In the pustule are seen the various stages of an acute exudative inflammation, which may be sero-fibrinous, hemorrhagic or necrotic.

Davaine, who studied excised lesions two and three days old, found the anthrax bacilli at the centre of the pustule, situated in the rete mucosum, in closely packed groups, separated by normal epithelium, the initial proliferation apparently taking place in the deep layers of the epidermis. According to Strauss, the black eschar is strictly dermic, consisting of the papillary layer and upper portion of the derma. It is covered by a crust composed of coagulated amorphous exudate, and is separated from the

underlying and living portions of the skin by a thick layer of embryonal cells, which form, as it were, a line of demarcation, in which the bacilli are found in very large numbers. The deeper skin and subcutaneous cellular tissues are distended by a sero-albuminous exudate, very rich in leukocytes. The infiltration is diffuse and not especially marked about the bloodvessels. The bacilli are found in the lymph spaces, not in the bloodvessels. In the neighborhood of the pustule, the papillary layer, the derma, and the subcutaneous tissues are the seat of an acute inflammatory œdema, with infiltration of the tissues by leukocytes and bacilli. In charbonous œdema, the bacilli are found exclusively in the subcutaneous cellular tissues—not in the skin, as in the malignant pustule.

**Distribution of Bacilli.**—In the lower animals the bacilli are found in the blood in enormous numbers. In man they are very much less numerous. They are always found in and near the point of inoculation, and in the lymphatic vessels to the nearest gland. They are generally found in the serum of the vesicles about the eschar, and sometimes in the œdematous tissues several inches away. In the late stages they may be found in the blood from the ear or fingers. They are generally present in the effusions into the serous cavities. When the kidneys are involved, the bacillus may pass into the urine.

Sections of the various tissues and organs yield very variable results in different cases. Some bacilli can usually be found, and sometimes large numbers.

**Symptoms.**—1. **External Anthrax.**—(*a*) *Malignant Pustule.*—This is the most common form in man, and is the result of direct inoculation. It occurs almost always on those portions of the body which are habitually uncovered, such as the face, neck, and arms. The lesion is usually single, though two and even three points of inoculation have been observed. The period of incubation is from one to three days.

At the point of inoculation a small red papule with a central punctum appears, sometimes preceded and always accompanied by itching and burning. By the second day a flattened vesicle has formed, which may be surrounded by some redness and swelling. The vesicle soon ruptures and is replaced by a yellowish erosion, which rapidly becomes brown and, by the fourth day, a black, depressed eschar has formed, surrounded by a very characteristic border of small vesicles. The circle of vesicles is slightly elevated, and may be complete or irregular. More or less numerous vesicles may appear on the neighboring skin. The eschar grows larger as well as deeper, and may attain a diameter of two to three centimeters. The subjacent and surrounding tissues are the seat of a hard œdematous swelling, which is often very extensive, involving an entire limb, the face, or a large part of the trunk. When the lesion is about the face, the deformity is very great. The neighboring lymphatics are sometimes involved, becoming tender and enlarged.

The freedom from pain in and about the lesions is remarkable. Even when very extensive, the patient complains only of a sense of weight and fulness, with some tenderness on pressure. Pus is never formed until the eschar begins to separate—from the ninth to the fifteenth day.

The general symptoms are very variable, and bear no relation to the extent of the local lesion. In severe cases the symptoms indicating general infection come on within twenty-four to thirty-six hours; in other cases not

for some days or even a week. The early symptoms are lassitude, malaise, headache, chilly sensations or slight rigors, loss of appetite, perhaps vomiting, restlessness, and disturbed sleep. Fever may be absent and is usually not marked.

The temperature is not an index of the gravity; it may be high in favorable and low in fatal cases. It frequently falls before death. The pulse may not be affected at first. It is usually more frequent, but soft. With the increase of gravity in the symptoms, it becomes weak, small, rapid and intermittent.

Among the later symptoms may be persistent vomiting; fœtid diarrhœa; a sense of oppression, with rapid breathing and a tendency to cyanosis; delirium, coma or convulsions, according to the internal localization of the infection. Consciousness is usually retained until the end. Death is sometimes sudden with no premonitory symptoms.

(*b*) *Malignant Anthrax Œdema.*—This form was first described by Bourgeois, and resembles the gelatinous œdema seen in many susceptible animals after inoculation. It is seen chiefly about the eyelids, though it may occur about the lips, neck and trunk. There is no characteristic eschar. The swelling may be very great and consists of a diffuse, painless, semi-transparent œdema, soft at first but growing harder as it increases. Vesicles may form on the surface, which are followed by eschars, similar to the ordinary malignant pustule. The course of the disease is more rapid and more fatal than in the ordinary form.

2. **Internal Anthrax.**—(*a*) *Intestinal Anthrax; Mycosis Intestinalis.*—This mode of infection is rare in man, but the usual one in cattle. The onset is sudden. There may be prodromal symptoms such as malaise, weakness, headache, chilliness, sweats, etc. Gastro-intestinal symptoms come on rapidly. There is complete anorexia and thirst, soon followed by nausea, persistent vomiting, diarrhœa—which may be bloody,—and marked abdominal pain. The symptoms have been mistaken for strangulation of the intestine. The abdomen becomes distended, the respiration rapid, dyspnœa is often considerable, due partly to areas of congestion in the lungs, or to pleural effusions, the pulse becomes rapid and small, the skin cold and clammy, the face cyanotic.

The temperature is seldom high, and usually only slightly above normal, often falling and becoming subnormal before death. The patient is profoundly adynamic and dies in collapse, retaining consciousness to the last; or else, delirium, convulsions, and coma may precede the end.

Death may take place in thirty-six to forty-eight hours, the symptoms resembling those of acute gastro-intestinal poisoning. The usual duration is five or six days.

(*b*) *Pulmonary Anthrax; Wool-sorters' Disease; Anthracœmia.*—In this the symptoms may be vague and slight until just before death, and even then the patient may not feel particularly ill. The patient may feel so little disturbance that no apprehension is felt, until suddenly he goes into collapse, becomes cold, pulseless, and dies within a few hours. The initial symptoms are malaise, slight chilliness or shivering, a sense of extreme weakness and fatigue, and uneasiness about the chest and stomach. Vomiting occurs in about one-half of all cases, and may be persistent. Diarrhœa is less frequent.

The lungs are always involved. There is a sense of constriction or oppression in the chest, with rapid and difficult breathing. Cough is generally present but seldom very annoying. The sputum is seldom abundant and

may contain blood or be rusty. Anthrax bacilli are sometimes found in it. The percussion sounds are often clear; impairment when present is usually on the right side. Moist rales may be heard. The right lung is more frequently and more extensively involved, as a rule, than the left.

The temperature is seldom very high. The pulse may not be much altered until late in the disease. As a rule, however, it is rapid and weak out of proportion to the apparent severity of the condition. Toward the end, it becomes small, irregular and rapid.

The urine is scanty, dark, and of high specific gravity—1,040 in some cases. It often contains albumin but seldom in large quantity.

The duration varies greatly. Death takes place, in the majority of cases, on the second, third, and fourth days. Bell has reported fulminating cases with death in seventeen hours.

**Diagnosis.**—In all forms of anthrax, the occupation of the patient should excite suspicion. Malignant pustule is almost always on some part of the body habitually uncovered. It is distinguished from furuncle and carbuncle by the absence of pain and suppuration. The absence of pain will serve also to differentiate it from phlegmonous erysipelas and cellulitis. When the lesion is fully developed the central, black eschar with the "brawny œdema," and surrounding vesicles are so characteristic that mistakes can hardly be made.

Intestinal anthrax is so much like other forms of acute gastro-intestinal poisoning that diagnosis may be impossible. There may be œdema about the root of the neck, which, with the occupation, may furnish a clue. Anthrax bacilli have been found in the serum before death.

Pulmonary anthrax is impossible to diagnose in the early stages. Bell says that the slightest illness in persons exposed to infection should be looked upon with suspicion until the possibility of anthrax is excluded. In cases which are not very rapid, and complicated with pleurisy and pneumonia, great prostration with a weak, rapid pulse, not accounted for by the local lesions, should attract attention. Diagnosis is difficult.

**Prognosis.**—This is bad in all forms. Cases in which the onset is marked by decided symptoms and a temperature above 102.5° F. are more favorable than those in which the symptoms are vague. The active symptoms indicate reaction on the part of the patient. The danger from malignant pustule varies with its site. Lesions on the neck are the most dangerous, on account of œdema of the larynx, and involvement of vital organs. Lesions on the eyelids are also especially fatal. Limitation of the lesions by marked inflammatory reaction about them is a favorable indication. Fever is more favorable than a low or subnormal temperature. Bell considers the pulse the best guide; when full and moderately rapid, the prognosis is hopeful. The outlook is bad when the pulse is small, weak and rapid.

**Treatment.**—Malignant pustule begins as a local infection, and for some days the bacilli are localized in and near the local lesion. Destruction of the pustule is therefore indicated, and it is of great importance that it should be practised at the earliest possible moment. When done before the bacilli have invaded the lymph channels and bloodvessels, a favorable issue may usually be confidently looked for. The actual cautery and excision with the knife are the two procedures most to be recommended. In either case extirpation must be thorough. After excision with the knife, which must include the tissues for at least a half inch beyond the eschar, the wound

should be well swabbed with carbolic acid. Injections of carbolic acid should be made into the tissues at five or six points around the wound and repeated at intervals of four hours if the symptoms are urgent. Bell advises for this purpose 15 minims of a 5 per cent. solution of carbolic acid in equal parts of water and ether. Over the whole should be applied an antiseptic dressing and an ice-bag.

In Europe, the actual cautery and chemical caustics are preferred. Among the latter, caustic potash is highly recommended. Graef has collected a series of 384 cases treated with caustic potash by himself and others with only 20 deaths. Muskett regards powdered ipecacuanha as having a specific action, using it as a dressing and also giving it internally. He treated 50 cases without a death in this manner. At Guy's Hospital, London, it is much used, although excision is first practised. The general treatment is supporting and stimulant.

There is little to be offered in the way of treatment in pulmonary and intestinal anthrax. Indications must be met as they arise, and the patient's strength kept up as far as possible by nutritious foods and stimulants.

**Serum Treatment.**—Marchoux[1] in France, and Sclavo in Italy, independently demonstrated in 1895 the possibility of producing a specific serum which is both prophylactic and curative, the former using rabbits and sheep, while Sclavo now uses the ass. Statistics of 164 cases treated with the serum give a mortality of 6.09 per cent. Legge[2] has recently (1905) collected the statistics of 65 cases in which Sclavo's serum was used, with 2 deaths. The average duration of treatment, estimated from 44 cases in which the data were precise, was eight days. Marked improvement was usually observed by the third day, as evidenced by arrest of development in the pustule, diminution of the œdema, and amelioration of the general symptoms. The initial dose should be large, as much as 40 cc., injected under the skin. A number of favorable reports of Sclavo's serum have been published in England.

**Preventive Measures.**—It is difficult to carry out efficient preventive measures. In some countries where anthrax is very prevalent, such as China, there is no way of getting reports of the existence or extent of anthrax, and no method of preventing the shipment of hides and hair from diseased animals packed with healthy material.

No efficient way has yet been discovered of disinfecting hides without destroying their commercial value. Porters handling such material should be required to have the arms and neck covered. In England, wool-sorters' disease has been lessened by regulations requiring that dangerous wools and hairs shall be steeped and washed in hot suds and sorted while damp. In other cases the sorting is done over wire screens provided with suction apparatus. The dust collected is burned. All skin, clippings, and bags which have contained dangerous materials, are disinfected before being sold. Operatives with sores or cuts are not allowed to work, and the proper appliances for disinfecting and treating such wounds are kept on hand in the workroom.

[1] *Annal. de l' Institute Pasteur*, 1895.
[2] *British Medical Journal*, 1905, I.

## RABIES.

**Synonyms.**—English, hydrophobia, madness; French, la rage, l'hydrophobie; German, Hundswuth, Tollwuth, Wuthkrankheit, Wasserscheu; Italian, idrofobia, rabbia, lyssa.

**Definition.**—Rabies is an acute, specific, rapidly fatal malady, communicated to man from some lower animal. It is always an inoculation disease, that is, communicated directly through a wound usually made by the teeth, the infective matter being the saliva, which contains the virus, the exact nature of which is unknown.

**Historical.**—Rabies in the dog appears to have been unknown to Hippocrates, but was distinctly described by Aristotle, 326 B. C., who recognized its transmissibility among animals, but denied its existence in man. He said, "Dogs are subject to rabies; it makes them furious; all the animals they bite while in this state become rabid, except man."

The earliest description in man is found in the first century of the Christian era, the term "hydrophobia" being used. This word is now properly restricted to the disease as seen in man. Celsus gave a good description of rabies in man, and advised suction and the actual cautery for infected bites. As early as 1591, transmission from wolves to man is recorded. Van Sweiten (1771) recognized the paralytic type in man, which was confirmed and more fully described in 1822, by Berndt, of Greifswald. The virulence of the saliva of dogs was first clearly demonstrated by Gruner and the Comte de Salm, in 1813. This was confirmed by Berndt, who held that the saliva of all animals affected with rabies contained the virus. By many it was believed that the herbivora were an exception to this, an opinion quite current until the work of Rey, in 1842, proved the correctness of Berndt's views. Our present ideas are largely due to the labors of Pasteur and his students, begun in 1881.

**Distribution.**—Rabies occurs in almost every part of the world, Australia being the only country known to be exempt, owing to the rigidly enforced quarantine. It is very rarely seen in Holland, Denmark, Norway, Sweden, and Switzerland. In France, Belgium, Hungary, and Russia, the disease is widespread. In the latter country it is common among wolves. It is quite common in Italy and Spain, although the official figures are small. In Germany, the disease is seen mainly on the frontiers and is rare in the interior. It is quite common in China and Japan. England is practically free at the present time. Rabies is common through the greater part of the United States, severe epidemics having been observed in several cities quite recently. The census for 1890 gave 143 deaths, distributed in 30 states, and for 1900, 123 deaths. These figures do not represent the full number of deaths from hydrophobia. Salmon collected statistics from the health officers of 73 cities which showed 230 deaths between 1890 and 1900.

**Animals Affected.**—All mammalia are susceptible and birds also contract rabies when bitten or otherwise inoculated. Dogs are most frequently affected, and to them we owe the perpetuation of the disease. It is not infrequent among wolves, foxes, hyenas, jackals, skunks, etc. Cats are rarely affected. Among the domestic animals cattle are most often affected, swine least so. It is uncommon in horses. The money losses from rabies are very heavy. In England it has appeared among the deer in parks and in 1889, out of 650 deer belonging to the Marquis of Bristol, 500 died in four months from rabies.

**Etiology.**—Hydrophobia being always the result of accidental infection from some lower animals, its incidence will follow closely that of rabies in the domestic animals, especially the dog, which is by far the most frequent source not only for man but for all other animals. Statistics of 16,172 persons bitten by supposedly rabid animals, collected at the Pasteur Institute, Paris, incriminate dogs in 15,021 cases, cats in 959, wolves in 14, foxes in 2, jackals in 9, horses in 32, asses and mules in 40, cattle 67, sheep 3, pigs in 12, and man in 13.

The danger following the bite of a rabid animal depends on the species, and the location and extent of the wounds. The bite of wolves is more apt to be followed by rabies than that of any other animal, owing partly to the greater activity of the virus, and partly to the savage mode of attack, the wounds being very extensive, lacerated, and often located about the head and face. Next in point of danger come bites from cats, then dogs, and lastly other animals. The report of the Pasteur Institute at Kharkoff for the ten years, 1892 to 1901, shows that, of 8,430 persons bitten by rabid dogs, 77, or 0.91 per cent. died, whereas of 193 bitten by rabid wolves, 32, or 16.58 per cent. succumbed to rabies.

There seems to be no authentic instance of the transmission of rabies through the bite of man, but in view of experimental evidence proving the virulence of human saliva for animals, such injuries must be regarded as dangerous, and be treated accordingly.

Bites on exposed parts of the body are more dangerous than those made through clothing, since the latter retains the virus, and the comparatively clean tooth enters the body. For the same reason long-haired dogs when bitten escape infection more often than short-haired ones.

Sheep are quite resistant to infection by bites, except after shearing. It has been shown by Pasteur, and Horsley, that rabbits which are shaven and exposed to the bite of a mad dog contract rabies more certainly and frequently than those bitten through the fur, even when the teeth penetrate deeply through the skin.

Bites in parts of the body having a rich nerve supply, as the face and hands, are particularly dangerous. In the former case especially, the virus is rapidly conveyed to the medulla. The same is true of bites in or about the large nerve trunks of the extremities.

The comparative danger is well shown in the statistics of 18,645 treated at the Pasteur Institute in Paris, as reported by Pottevin.

| Location of Bite. | Number Treated. | Deaths. | Per Cent. |
|---|---|---|---|
| Head | 1,608 | 21 | 1.36 |
| Hands | 10,254 | 49 | 0.47 |
| Limbs | 6,783 | 20 | 0.29 |

Interesting figures on the same point are given from the Pasteur Institute at Kharkoff for the years 1892 to 1901.

| Location of Bite. | Number Treated. | Deaths. | Per Cent. |
|---|---|---|---|
| Upper extremities | 5,301 | 34 | 0.64 |
| Lower extremities | 2,601 | 2 | 0.08 |
| Head and face | 946 | 73 | 7.72 |
| Body | 542 | 0 | 0. |

Rabies may be transmitted by the deposit of saliva containing the virus on abraded surfaces, as by licking. It may also be contracted through wounds received in making autopsies on animals or persons who have succumbed to the disease. In all cases a solution of continuity is necessary for the absorption of the virus; it cannot pass through the healthy skin. It is doubtful if the virus can be absorbed through the digestive tract.

Not every person bitten by a rabid dog becomes infected. Leblanc, as the result of careful investigation, gives 16.6 per cent. as the proportion, an estimate which is generally accepted as conservative and correct. Some series of cases show much higher figures. Bouley reports 152 deaths among 200 persons bitten, but of these, 120 were bitten on the face and hands, the greater danger from which has been noted. The mortality following bites of rabid wolves is variously estimated at from 60 to 80 per cent.

**Sex.**—Men are not only more liable to be bitten by rabid animals, owing to their various callings, but when bitten are more apt to contract hydrophobia. This is doubtless due to the greater protection afforded by the skirts, and not to any inherent immunity in women.

**Age.**—Two-thirds of all cases occur in children under fifteen years of age, according to Bollinger. Children of both sexes are particularly liable to bites, owing to their habit of collecting together for play in the streets, their inability to recognize danger, and their lack of defence. For obvious reasons they are often bitten about the face. On the other hand, they appear to enjoy considerable relative immunity. Brouardel says that of every 100 persons below twenty years of age bitten, 31 die, while above this age, 62 of every 100 die.

**Influence of Season.**—The statistics of the Pasteur Institute, Paris, from 1886 to 1893, show that the largest number of patients apply for treatment in March, April and May; the smallest in September, October and November.

The statistics of the Pasteur Institute at Lille for seven years, 1895 to 1902, show the following results:

| | | | |
|---|---|---|---|
| January | 141 | July | 169 |
| February | 111 | August | 139 |
| March | 144 | September | 111 |
| April | 149 | October | 146 |
| May | 143 | November | 148 |
| June | 175 | December | 173 |

A table compiled by D. E. Salmon, including 14,961 cases of canine rabies, gives the following results by months: January 8.6, February 7.4, March 9.0, April 8.8, May 9.4, June 9.6, July 9.6, August 9.4, September 9.4, October 8.6, November 9.0, December 7.7. It is seen that more cases occur from April to September, inclusive, than during the rest of the year, due, no doubt, to the fact that dogs are more apt to run abroad during the warm season than during the winter months.

**Virus—Distribution.**—The virus is always present in the saliva and appears to be excreted chiefly by the parotid glands, though not entirely so. The salivary glands themselves are virulent, though not so constantly as the saliva. The saliva of the dog has been shown by Nocard and Roux to be always virulent twenty-four to forty-eight hours before the animal shows any symptoms of illness. The lachrymal glands, the mucous and subarachnoid spaces may contain the virus. It is also excreted in the milk of

times. The blood and lymph are never virulent, and Helman has shown that it is absent from the lymph glands in relation to the point of inoculation. The muscles and organs are innocuous.

Every part of the central nervous system constantly contains the virus, but it is especially concentrated in the medulla. The large nerve trunks are usually virulent, as is also the cerebrospinal fluid. Pasteur showed that the "entire nervous system, from centre to periphery, is capable of cultivating the virus." Roux found that the peripheral nerves, even on the side opposite inoculation, were often virulent.

**Nature.**—The exact nature of the virus is unknown. The behavior of the disease makes us certain that it is caused by a specific microörganism, which, after introduction into the body, undergoes a period of incubation, during which it multiplies and produces a toxin having a special action on the central nervous system, as is the case in tetanus, to which it bears a striking analogy. Nocard in 1880, and Paul Bert in 1882, showed that, on filtration through plaster, the virus was held on the filter, the filtrate being devoid of pathogenic power. Further studies by di Vestea, Bertarelli and Volpino, Celli and Blasi, Remlinger and others, have shown that the virus will frequently pass a coarser filter, such as the Berkefeld V, and will sometimes penetrate a Chamberland F, under pressure. Several observers have found that the filtrate frequently produces cachetic and paralytic phenomena not unlike rabies in dogs and rabbits, but after death the medulla of the animal is incapable of injuring other animals, showing that the condition is a toxic one. In this respect also the analogy to tetanus is close, and from this fact the disease has been considered a toxoneurosis. It is further known that serial passages through susceptible animals increase the power of the virus, while it is attenuated by drying, heat, light, etc., as many bacteria are.

Innumerable attempts have been made to discover the causative agent, and, from time to time, observers have announced the finding of cocci, bacilli, yeasts, and protozoa which they believed to be the pathogenic organism. None of these discoveries have stood the test of rigid investigation. At the present day, the opinion is growing that rabies is due to a microörganism of the ultra-microscopic class, but considering our lack of definite knowledge, all opinions must be accepted with reservation.

**Resistance.**—The virus is destroyed by heat, drying, and light. In dry air, protected from the light and from putrefaction, the spinal cords of rabbits lose their virulence gradually in fourteen to fifteen days, a fact made use of by Pasteur in preparing his vaccines. When in thin layers, the virus is entirely destroyed by drying in four to five days. Direct sunlight destroys it in about forty hours. In water the virus retains its power for twenty to forty days, or longer. Neutral glycerine preserves it unchanged for a long time. Roux found that after four weeks in glycerine at 30° C. the virus was unchanged in pathogenic power.

Galtier has found the virus active in the central nervous system of rabbits buried for twenty-three days, of sheep buried thirty-one days, and of dogs buried forty-four days. It is not injured by cold, resisting the prolonged application of a temperature 10° C. to 20° C. below zero. It is destroyed by a temperature of 50° C. in one hour, or 60° C. in a half hour.

Investigators differ greatly as to the effects of various antiseptics. The best appear to be corrosive sublimate, 1 to 1,000, citric acid in 6 per cent. solution, and saturated watery solution of iodine. The virulence of fixed

virus is destroyed in eight minutes by 1 part of a 5 per cent. solution of formalin to 3 parts of virus. Mixed in equal parts it is destroyed in five minutes. Bile rapidly destroys the activity of the virus. When an emulsion of the bulb from a rabid animal is mixed with an equal volume of bile from either a healthy or rabid rabbit, and allowed to stand a few minutes, it may then be inoculated without danger of causing rabies.

**Penetration.**—From the point of inoculation the virus makes it way to the central nervous system along the nerve trunks, producing no symptoms until the central system has been the seat of the virus for some time. If the spinal cord of an animal is cut, and a virulent inoculation then made in the hind extremity, it will be found, after a suitable period of incubation, that the spinal cord below the point of section is virulent, while above, it contains no virus. When the inoculation is made into the brain or upper extremity, the descent of the virus can in like manner be prevented by section of the cord. Roux has shown that in rabies developing slowly after inoculation of the limb on one side, the virus may also be found in the peripheral nerves of the opposite side; if, however, the period of incubation is short, only the nerves on the wounded side contain the virus. Clinically it has been observed that the paralytic and convulsive phenomena are more marked on the side of the inoculation. It is said by di Vestea and Zagari that paraplegia is apt to follow bites of the lower extremities, while the furious type of rabies is produced by bites of the head and upper extremities. Experimentally in small animals the circulation and lymph channels appear to play some part in the absorption of the virus.

**Incubation.**—The average period in man is about forty days, but it varies between wide limits. The great majority of cases occur between the twentieth and ninetieth day. Cases have been reported as developing several years after infection but are generally discredited. Gowers says, "It is, however, certain that the disease may occur after an interval of a year or eighteen months, and it is difficult, therefore, to deny the possibility of a longer interval." The shortest period of incubation is about twelve days. The development of rabies is not common after three months, and is quite rare after six months.

**Pathology.**—There are no characteristic gross pathological changes. In man, congestion of the lungs and emphysema are common, due to the convulsive seizures. The muscles of the chest and pleuræ are sometimes ruptured in the same way. Congestion of the fauces, œsophagus, stomach and larynx is commonly found. Of the internal organs, the kidneys and spleen most often show congestion. The brain and spinal cord frequently show marked congestion. The blood generally remains fluid after death and is dark in color.

**Pathological Histology.**—In 1872, Nepveu described the findings in a case of human rabies observed by Pollailon and himself. They noted that the whole cerebrospinal axis was strongly congested and that the Gasserian ganglion was hyperæmic and infiltrated with round or oval cells, some hyaline in appearance, and which they considered "probably epithelioid cells from the capsule of the ganglion cells." In the same year, Clifford Allbutt described changes observed in the cerebrum, medulla, pons, and spinal cord, which pointed "to the action of an animal poison acting primarily on the cerebrospinal nervous system." Many authors have described lesions of the nervous system which have been thought more or less characteristic.

Gowers found distinct morbid changes in 7 out of 9 cases. He describes "dilatation of the small vessels, accumulation of leukocyte-like corpuscles around them and in the tissues, clots in small vessels evidently formed during life, and minute hemorrhages." These changes were found in the cortex of the hemispheres, medulla oblongata, and the spinal cord, but were most intense in the medulla, especially about the nuclei of the pneumogastric, hypoglossal, and spinal accessory nerves. He observed marked packing of leukocytes about the vessels, which many times were so numerous as to entirely fill the perivascular lymphatic sheath, and even extend into the adjacent tissue. About the nuclei were found dense collections of corpuscles which he considered identical with pus cells, and hence called them "miliary abscesses." He did not consider the lesions pathognomonic in their character, although their intensity and distribution were peculiar to rabies and constituted a distinguishing anatomical character.

Babes has described what he considers the essential lesion of rabies,—an accumulation of embryonic cells in the neighborhood of the central canal, and especially about the large modified cells of the motor centres of the bulb and cord. In the bulb he describes the pericellular accumulations of embryonal cells found by Kolessnikoff, for which he proposes the name "rabic tubercle." The cells of the bulbar nuclei undergo degeneration and show the various stages of chromatolysis. There is loss of the prolongations and progressive modification with even total disappearance of the nuclei, a dilation of the pericellular space, and an invasion not only of this space, but also of the nerve cells by embryonal cells; at the same time, there appear small corpuscles which are hyaline, brownish, and in parts metachromatic. Many of the nerve cells become surrounded by a large zone of embryonal cells, degeneration of the cell follows, and when complete the embryonal cells occupy the cell area entirely, forming the "rabic tubercle." Babes has for many years made routine examinations of the bulb of all cases for the purpose of diagnosis. Reporting on the bulbs of 487 dogs, all of which were controlled by inoculation of rabbits, he finds the lesion so constant that he regards it as diagnostic of the disease.

In 1900, Van Gehuchten and Nélis discovered what they believed to be the diagnostic lesion of the disease. While recognizing and confirming many of the lesions described by other writers, they consider them secondary and of little importance. They believe that the virus acts by preference on the peripheral cerebrospinal and sympathetic ganglia. The most constant and marked lesions are found in the intervertebral and the pneumogastric ganglia. They consist of the atrophy, the invasion, and the destruction of the nerve cells by new-formed cells, due to the proliferation of the cells of the endothelial capsule. The new-formed cells increase in number, invade the protoplasm of the nerve cell, and finally occupy the entire capsule, the nerve cell proper having completely disappeared, while in its place is seen a mass of round cells. The nerve cells which are not destroyed may show various degenerative changes of the protoplasm and nuclei, such as vacuolation, eccentricity of the nuclei, chromatolysis, etc. In advanced cases practically all the nerve cells may be destroyed, and the section has much the appearance of an alveolar sarcoma. These changes have been found in a great variety of animals. They are best observed in dogs and cows, but are quite characteristic in all animals studied.

In 1903, Negri announced the discovery of certain bodies in the nerve cells of rabid animals. They are found especially in the horn of Ammon. They are from 1 to 23$\mu$ in diamater, oval, round or triangular in shape, according to their size and position in the cell. They are strongly eosinophilic.

The Negri bodies are described as consisting of a fundamental substance, which is homogeneous, non-granular and hyaline in appearance, resembling coagulated albumin. Within them are clear, shining areas, which at first sight appear to be vacuoles, but under higher powers show one or more points of deeper color. They are quite resistant to external agencies, remaining unchanged for a long time by putrefaction, desiccation (183 days), etc. Material may be preserved in glycerine for eighty days without altering the Negri bodies. They are destroyed by 33 per cent. solution of caustic potash.

They are well brought out by dilute solutions of acetic acid or by 10 per cent. osmic acid, or by immersion in 33 per cent. alcohol for forty-eight hours, or by staining after the method of Mann or Romanowsky. They are especially numerous and large in cases of rabies of long incubation period (Negri). They are best developed in the horn of Ammon, less in the cells of Purkinje, and less still in the spinal ganglia and vagus.

The nature of the bodies is unknown. Negri believes them to be protozoa, and considers them the causative agents of the disease. Valenti reports that the virus of rabies is neutralized in the test-tube as well as the living body by quinine, while no other alkaloid was found which had this power. This is held as strong evidence of the protozoan nature of the bodies.

Babes has made an exhaustive study of the matter and confirms the practically constant presence of Negri bodies in the brain in rabies, although he does not consider them the actual parasite, but rather evidence of the resistance on the part of the cell, by which it is able to englobe and encapsulate the invading organism. He believes the fine round granules coloring a blue or black with the Cajal-Giemsa stain to be the parasite in its active state. These granules are found exclusively in the protoplasm of the degenerated nerve cells in the most severely involved areas of the nervous system, whereas the Negri bodies occur in cells but little altered and having no close connection with the symptoms. He believes the Negri bodies to be encapsulated parasites undergoing involution or degeneration.

**Postmortem Diagnosis.**—There are no gross lesions, either in man or in animals, which enable one to state positively that death has been due to rabies. In dogs, perhaps the most constant feature is the absence of food from the stomach and the presence of foreign matter, such as straw, wood, hair, etc. Axe found this condition in 90 per cent. of cases. Emaciation is usually marked and putrefaction takes place rapidly.

Until recently we have been obliged to resort to inoculation of animals for a positive diagnosis. Rabbits are usually selected, and the inoculation made under the dura, since infection is more rapid and certain than when the inoculation is made elsewhere. Symptoms appear from the sixteenth to the twenty-first day, as a rule, but may be delayed for sixty days. The type of rabies following inoculation is usually the paralytic, though rarely the furious type is seen. The virus of rabies is concentrated in the medulla, and especially in the floor of the fourth ventricle. For inoculation the tissue is by preference taken from this area.

**Microscopic Diagnosis.**—On account of the time required, the inoculation of animals is of no service in determining the necessity of antirabic inocu-

lations. The treatment is usually completed before an opinion can be given. Fortunately it is now possible to make a rapid diagnosis by microscopic methods, owing to the discoveries of Van Gehuchten and Nélis, and Negri, already described. For diagnosis by the method of Van Gehuchten and Nélis, the plexiform ganglion of the pneumogastric nerve is selected, as it is easily dissected out, and presents the characteristic changes in the ganglion cells. In dogs, the ganglion is readily found by cutting down on the pneumogastric nerve in the neck, and following it up. Near the skull it divides into two branches, on one of which, the smaller, is found a small, oval, reddish ganglion, the cervical. The larger branch enters the plexiform ganglion, which is easily recognized by its fusiform shape, and white or grayish color. It is seldom more than a half inch from the foramen, and it is generally necessary to cut the nerve as it emerges from the skull. The ganglion may be prepared for section by any of the rapid methods.

The best stain for general use is hemalum (Grubler) made up with a 0.5 per cent. solution of carbolic acid, and counterstained with eosin. This method has been in use at the laboratory of the State Live Stock Sanitary Board of Pennsylvania for five years, and has been found most satisfactory. A large number of cases have been controlled by inoculation, and no error has yet been found. While the lesions cannot be considered specific, since similar changes have been noted occasionally in other toxic conditions, and in the ganglia of aged dogs, yet by their extent and constant occurrence in rabies they have an unquestionable significance, and, taken in connection with even a meagre history, have an absolute diagnostic value.

Certain precautions must be observed: The animal must be allowed to die of the disease. The lesions may be slight or entirely wanting in animals killed prematurely, and in such cases their absence does not preclude the existence of rabies. If absent after death from the disease, we can positively deny the existence of rabies.

A diagnosis can be made within twenty-four hours by rapid fixation and mounting, and is easily made within forty-eight hours.

The diagnosis by the method of Negri has advantages over the above in that the Negri bodies are usually found early in the disease, are not affected by putrefactive changes incident to delay in obtaining the material, and the technique is more simple. In practice a small portion of the brain should be taken from the cortex of the cerebellum, and also from Ammon's horn, as the bodies may be numerous in one area and not in the other. The pieces of tissue may be fixed in Zenker's fluid, embedded in parafin, and stained with eosin and methylene blue. The bodies show red against the blue background of the cell. The stains of Mann and Romanowsky are especially recommended.

The process of hardening and cutting may be dispensed with and the examination for Negri bodies made directly in the fresh tissues by the smear method, which has been found very satisfactory. It has the great advantage of giving practically an immediate diagnosis. It is described by Gorham as follows: The top and occipital portions of the skull are removed, and, without taking out the brain, pieces 3 to 4 mm. in diameter are taken from the cerebral cortex in the region of the crucial sulcus, the cortex of the cerebellum, and the hippocampus major. These are placed on a well-cleaned slide and crushed under a cover-glass until the matter spreads to the edge of the cover, which is then drawn slowly and evenly the length of the slide,

leaving a uniform film of brain matter. The slide is then immersed in wood alcohol for one to three minutes and dried in the air. The stain is made by adding 2 drops of a saturated alcoholic solution of rose aniline violet, and 16 drops of a one-half saturated aqueous solution of methylene blue, to 18 cc. of distilled water. Flood the slide with this stain and heat gently until steam rises, wash in water and dry. The Negri bodies appear as pink, crimson or magenta inclusions in the blue nerve cells. The color taken depends on the condition of the material and the proper mixture of the stains. In early cases the bodies are found only in the large cells, while in advanced cases they are found in all kinds of nerve cells.

Volpino's osmic acid method is rapid and simple. A portion of the horn of Ammon is removed and cut into segments 3 to 4 mm. thick, which are put into test-tubes containing 4 to 5 cc. of a 1 per cent. solution of osmic acid. After five to six hours or longer, they are removed and washed in water for a half hour, then put into absolute alcohol for three to four hours. They may then be cut by hand and mounted in glycerine. It is not necessary to harden the tissue, since a fairly thin section can be readily pressed out on the slide. The preparation is brownish in color, the cells are light coffee-color, the nuclei paler, and the nucleoli strongly colored. The Negri bodies are seen in the cells, and resemble nucleoli. There may be one or several to a cell.

The discovery of Negri has been abundantly confirmed, and while the etiological significance, as well as the nature of the bodies is still in doubt, they have been shown to be very valuable for the purpose of making a rapid histological diagnosis. Bertarelli states that in more than 1,000 examinations the Negri bodies were never found in animals free from rabies, and, on the other hand, were present in all infected animals, with three exceptions. Poor, at the Health Department Laboratory, New York, has examined material from 17 cases of rabies from natural infection, 16 cases of the inoculation disease, and 22 controls. The Negri bodies were found in all cases of natural infection, and in all of the inoculation cases except 1 dog which was killed on the first appearance of nervous symptoms. Among the controls 1 case of experimental tetanus showed a few minute eosinophile bodies in the Purkinje cells of the cerebellum, which, however, could be differentiated from the Negri bodies. He confirms fully the diagnostic value of the method.

**Symptoms.**—As a rule, there are no symptoms during the period of incubation. The wound generally heals as any other similar injury without local thickening or glandular involvement. In some cases mental depression is marked, but it is usually due to anxiety and apprehension rather than to the disease. Instances have, however, been reported by most reliable observers, in which mental symptoms were noted in children too young to be apprehensive of danger, and in persons who were not aware that they had been bitten by a rabid dog.

Three stages are usually recognized, but they are not always well defined. The symptoms marking the later stages are frequently prominent from the first.

1. **Premonitory Stage.**—This is often marked by irritation, tingling or a feeling of numbness at the seat of the bite, or else there may be quite severe pain, lancinating in character, and radiating up the limb. These sensations may exist for as much as a week before other symptoms appear, although usually this stage lasts only twenty-four to forty-eight hours. The patient complains of general malaise, depression and melancholy, with extreme

anxiety and a sense of impending danger. The sleep is disturbed; often there is great restlessness and irritability. The sensibilities are often very acute; there may be hyperæsthesia of the skin, photophobia, etc.

About this time symptoms referable to the throat appear, such as slight difficulty in swallowing liquids, or a slight choking sensation. The voice becomes husky, often there is precordial distress, with a sense of oppression, the patient frequently taking deep inspirations. Slight fever, with increase of pulse rate is commonly present; occasional rigors occur.

During the early stages of the disease many patients show symptoms very much like those characteristic of rabies in the dog: an unnatural suspicion, irritability of temper, surliness, desire to be alone, alternating with periods of mental excitement and loquacity. Delusions and maniacal delirium appear as late symptoms.

2. **Stage of Excitement.**—The symptoms all increase rapidly in severity. The face takes on an expression of terror with marked pallor; the muscles are drawn and restless; the eyes have a "hunted look." There is intense thirst, but every attempt to swallow water brings on a spasm of the muscles of deglutition and respiration,—the typical hydrophobic spasm. The extreme thirst impels the patient to make strong efforts to drink. The water is taken into the mouth, but as soon as it touches the fauces, it is expelled with considerable force, and violent spasmodic contractions of the muscles of deglutition and respiration come on. These attacks are accompanied by a sense of extreme dyspnœa, "even when the glottis is widely opened or tracheotomy has been performed." They increase both in intensity and frequency, and there develops a cutaneous hyperæsthesia, in consequence of which the slightest draught of air, or contact with anything cold, is sufficient to determine an attack. The suffering of the patient, both physical and mental, is intense during the spasms, and the dread of them produces a mental condition which increases the ease with which they are excited. The hypersensitiveness is so marked in some cases that the sight or sound of water, or even the verbal suggestion of it, a strong light, or the reflection from a polished surface or looking-glass, is sufficient to bring on a spasm. To this dread of water, acquired by experience of its effect, is due the name "hydrophobia." In man these spasms constitute at once the most distressing feature of the disease, as well as the most diagnostic symptom.

With the advance of the disease, the convulsive attacks, which were at first confined to the muscles of deglutition and respiration, involve other groups of muscles and become general. They may be tetanoid with marked opisthotonos and suspension of respiration, or else be "coördinated and closely resemble hysteroid convulsions." Not only is the frequency and intensity of the seizures increased, but the length of the paroxysms often becomes greater and death from asphyxia may occur. They may still be caused by any of the excitants mentioned, but more often come on without appreciable cause. The skin and patellar reflexes are usually increased in this stage. Much distress is frequently caused by auditory and olfactory hyperæsthesia. Slight odors precipitate attacks of sneezing and even convulsions.

The mucous surfaces are covered with thick tenacious mucus; the saliva is abundant and viscid, while inability to swallow it is often present. There are constant attempts to expel it, which are only partially successful, so that it hangs from the patient's mouth. Vomiting is frequent, the ejected fluid being greenish-brown and sometimes containing blood.

The horror of the convulsive attacks is so great that delusions or even maniacal delirium often appear. The delirium is most marked during the paroxysms; the patient may throw himself from the bed, and even inflict severe wounds on himself without apparent pain. He may attempt to bite his attendants or spit at them. During the convulsions noises are made in the throat which have often been described as resembling the bark of a dog. The delirium is not constant. During the intervals the patient can be brought to consciousness and even reason by his attendants. He often shows anxiety for the safety of those about him, begging to be restrained from injuring them.

The duration of this stage is from one and a half to three days.

3. **Paralytic Stage.**—The convulsive attacks, with the attendant mental symptoms, usually abate a short time before death, a paralytic condition taking their place, and the patient sinks rapidly, dying from exhaustion. Coma may precede death.

*Temperature.*—Babes lays stress on an elevation of temperature during the period of incubation. This has often been observed in animals, but its constant occurrence in man remains to be proven. In the early stages, elevation of temperature is lacking or moderate, and throughout the disease may not exceed 100° or 101° F. Usually the temperature rises as the symptoms increase, reaching 103°, 104°, 105° F., or even more, just before death, and may continue to rise after death for a short time.

The urine frequently contains albumin, sometimes sugar and blood.

The pulse is quick throughout. During the last stages it becomes more quick, small in volume, and irregular. Increased sexual desire is not infrequent in the early stages and may increase as the disease advances. Persistent priapism with emissions may add much to the difficulty of urination.

**Paralytic Rabies.**—Sometimes the convulsive attacks, the excitement and delirium, and the hydrophobic spasms are entirely lacking, and we have typical paralytic rabies, so often seen in dogs and in animals inoculated experimentally. This type is especially apt to follow extensive bites where the amount of virus is large. According to di Vestea and Zagari, it is apt to follow bites about the lower extremities, while the furious type is usually the result of bites about the head and hands. The first symptoms are usually in the bitten limb, but sometimes violent pains extend from the lower trunk down the limbs, which feel heavy and difficult to move. Paraplegia soon comes on, and may be the first symptom. The course of the disease is an acute ascending paralysis, involving the sphincters and the muscles of the trunk, and ending in death by paralysis of the muscles of respiration, or by cardiac syncope. Diagnosis may be impossible except by inoculation of animals, and microscopic examination after death.

**Duration.**—Death usually occurs between the second and fifth days; rarely the patient may survive eight or nine days. Bouley found that of 90 cases, 74 died during the first four days—most of them on the second and third days. In 16 cases life was prolonged beyond the fourth day.

In the paralytic type death often does not take place until the seventh day.

**Rabies of the Dog.**—The disease is seen in two types, a furious, and tranquil or paralytic type.

*Furious Type.*—In the furious type the first symptoms consist solely in changes in disposition, manifested by distress or uneasiness, and restlessness.

The animal is always easily excited. At this stage, he does not usually show a disposition to bite; he is still docile and obeys orders, though not so quickly as in health; he soon seeks solitude and shows a disposition to hide in dark corners, or burrow in the straw of his kennel; periods of calmness alternating with marked excitement are observed; he still shows affection for his master and may respond to caresses even more affectionately than is his wont. He may, however, be irritated by strangers, or, being surprised by touch or blow, may inflict a bite. The appetite is still good and may be excessive. Soon the restlessness becomes more marked; the dog is constantly in motion; he is apt to tear carpets, rugs, etc., which may be in the room with him; he shows signs of delirium, looking off into space apparently seeing some imaginary object; at times he will attack an imaginary enemy. He will still respond to his master's voice, but his attention cannot be held for any length of time. At this early stage, the voice becomes modified, and this may be regarded as one of the most typical symptoms. Instead of the clear and sharp bark which is natural, the latter part of the note becomes prolonged and of a higher pitch, going off into a plaintive cry, which has been likened to that of a dog fatigued in the chase, and in succeeding short barks which may follow, the jaws do not close completely as in ordinary barking.

While this symptom is a striking one and quite constant, it may be lacking at times and certain dogs remain quiet in spite of all attempts to excite barking. The appetite diminishes about this time; food is taken with more or less difficulty, and soon it is refused, swallowing having become painful and difficult. The animal may appear to have a bone stuck in its throat, a symptom which often tempts the owner to make the dangerous examination for some obstruction. There is no fear of water, and the animal drinks water and other liquids quite greedily, until paralysis of the constrictor muscles of the pharynx makes swallowing impossible.

The excitement becomes marked and the animal is now furious. If a stick or other object is presented to him, he seizes it with power, and attacks the bars of his cage. If at liberty, he attacks everything in his way, swallowing all sorts of articles, such as wood, paper, straw, and stones, the presence of which in the stomach after death is one of the most striking postmortem features of the disease. At this time he begins to wander, running with his tail hung, the mouth open, and the eyes with a wild look; he attacks every object or animal which comes in his path. As a rule he runs straight ahead and does not turn out of his way to attack animals. The dog may travel tremendous distances, but is apt to return to his home, exhausted and covered with dust and blood; or else he may continue his course until he falls exhausted, as many as fifty miles being covered. Very soon paralysis sets in, commencing in the hind legs, and finally becomes general. The dog is no longer able to stand; weakness becomes more marked and stupor sets in, from which the animal may be aroused, but which becomes deeper and deeper and ends in death. The course of the disease is always rapid, covering from six to ten days, and averaging from four to five days. The symptoms are so characteristic that once seen can scarcely be mistaken for any other disease. The furious type just described is the most common.

*Paralytic Type.*—The paralytic type, ordinarily spoken of as "dumb rabies" constitutes from 15 to 20 per cent. of all cases. In certain countries, as in Turkey, it is the prevailing type, which explains the relative rarity of

rabies in man in this country where dogs abound. The commencement of the disease is the same as in the furious type, but the accesses of fury are lacking. For several days the dog appears restless, seeking seclusion and dark places: The paralysis may commence in various parts of the body, but, as a rule, affects first the muscles of the jaw, which soon drops, the dog being unable to close its mouth, and the tongue hanging out; the whole expression of the animal is pitiful in the extreme; an abundance of saliva runs from the mouth; the taking of water is impossible; the mouth becomes dry, covered with dust, and brownish in color. The animal is quiet; he does not respond to provocation, nor does he seem to wish to bite. The progress of the disease is more rapid than in the furious type. The paralysis extends, and death occurs on the second or third day.

Other cases are observed in which the type of the disease is more or less intermediate between the two just described. There are some in which a very short period of fury is followed by a rapid paralysis, while in others the paralysis is more slow in its progress and the animal shows a slight disposition to attack when irritated. In the "dumb" type of the disease it is common to suspect an obstruction in the throat, and in the attempt to locate it the saliva may infect wounds of the hand. The animal never wanders and, being unable to bite, the danger of transmission is slight.

**Diagnosis.**—Hydrophobia may be confounded with tetanus, hysteria, acute mania, and lyssophobia.

From tetanus it is distinguished by the longer period of incubation, the absence of trismus and the "risus sardonicus," and the complete absence of spasm during the intervals. The mental condition is different; the anxiety and the restless irritability so characteristic of hydrophobia are lacking in tetanus. The most characteristic symptom of hydrophobia, which is lacking in tetanus, as well as the other diseases, is the respiratory spasm excited by attempts to swallow water. Hysteria sometimes simulates hydrophobia quite closely, especially in cases where the patient has been bitten by a dog and has been anxious about it. In these instances there may be general convulsions with constant barking and biting. A careful review of the history and symptoms, and especially the absence of the respiratory spasm, will usually make the diagnosis clear.

The differentiation from mania may be difficult at first, and must depend largely on the history. The rapid course of the disease will soon clear up the diagnosis. As Gowers says, "No patient ever passed from mental health to a state of imminent danger in two or three days in consequence of simple insanity."

Lyssophobia is the name given to a series of symptoms which are sometimes seen in nervous persons who have an exaggerated fear of hydrophobia. Auto-suggestion determines spasms in the throat on swallowing, and a dread of water may follow in consequence. The symptoms usually occur soon after the bite, sooner in fact than the shortest period of incubation in the true disease. There is lacking also the true respiratory spasm, and the patient can usually be quieted by simple treatment. It has not been proven that death ever takes place from lyssophobia.

**Prognosis.**—Instances of recovery have been reported, but at best are so rare that a fatal outcome must always be looked for. In dogs a few well authenticated instances of recovery following inoculation have been reported.

The prognosis as regards bites by rabid animals, depends, as has been stated, on the animal inflicting the bites, the size, number, character, and location of the wounds. It depends also on the length of time which elapses between the injury and cauterization, and on the thoroughness with which it is done. When done properly and thoroughly the protection is very great—in moderate wounds practically absolute. The statistics of Proust show that, in a series of 117 cases, which were not cauterized, there were 96 deaths; while among 249 cases, in which cauterization was practised, only 89 deaths occurred. When the wounds are multiple and lacerated, and especially when about the face and head, thorough cauterization is difficult or impossible.

The outlook is most favorably influenced by the Pasteur treatment. At the parent Institute up to January, 1904, 27,719 cases of all descriptions have been treated, with 117 deaths, a mortality of 0.42 per cent. These figures exclude a small number of persons in whom the disease appeared during or within fifteen days after treatment.

As in other methods of vaccination, immunity is produced only after a certain lapse of time, and in cases of short incubation, or of late commencement of the treatment, the disease may manifest itself before the vaccinal effect has been procured. For this reason certain cases of death are justly excluded from the statistics of the Pasteur treatment. Their admission would, however, raise the percentage very little. The recent work of Krauss and Kreissl throws much light on the production of immunity in man by the Pasteur treatment, and emphasizes the importance of beginning treatment promptly. These authors find that the serum of healthy men, as a rule, does not contain any protective property against the virus of rabies, nor is any found immediately after the completion of vaccination, but twenty-two days later marked antirabic power is present, and is retained for a long time. Cases in which the treatment is unsuccessful are probably due to the absence of this property. It is important that the treatment be begun within one week of the bite. Statistics collected by Högyès, including 54,620 persons treated at 24 institutes, show that the total mortality was only 0.77 per cent. These figures prove, moreover, the harmlessness of the treatment.

In Hungary, where rabies is very prevalent, from 1890 to 1895 there were 5,899 persons bitten, of whom 4,914 received the Pasteur treatment, with a mortality of 1.20 per cent., while among those not treated 14.94 per cent. died of rabies.

**Treatment.**—When the disease has declared itself, the treatment is purely palliative, and directed to relieving as far as possible the suffering of the patient. Our efforts must be directed to preserving the strength, and lessening the frequency of the paroxysms. Every source of annoyance, physical and mental, should be removed. The room must be darkened, warm, and quiet. Only the necessary attendants should have access to the patient. Especially must draughts of air and sharp noises be avoided. The diet should be as concentrated as possible, and liquid. Osler advises the use of cocaine to the fauces to facilitate the taking of liquids. If the dysphagia is marked, recourse must be had to rectal enemata. Thirst must be relieved by the same measures.

The list of drugs which have been recommended is a long one. None have any specific value. Hypodermic injections of morphia and inhalations of chloroform will generally give more relief than any other drugs. They should be used from the beginning, and no time wasted by giving the milder

antispasmodics. Calabar bean and curara have been recommended. Three cases of cure are credited to curara, one of which Gowers considers "undoubtedly genuine." As it acts by paralyzing the motor nerves, artificial respiration may become necessary.

Forcible restraint during the paroxysms is often required. Tracheotomy has been advised, but is useless, since the dyspnœa is due to spasm of the respiratory muscles, and the glottis is not closed.

**Preventive Treatment.**—The bite of any suspicious animal should receive prompt attention. The invariable rule must be: Cauterize as soon as possible and in the meantime do everything to get the virus out of the wound and prevent its absorption. Open the wound freely so that every part of it can be exposed. Encourage bleeding by cupping or suction with the lips, the mouth being well washed after each application. Bathe abundantly, preferably with tepid water. If the wound is on a limb, a ligature may be applied above the site. As soon as possible the wound must be thoroughly cauterized. For this purpose fuming nitric acid is the best agent. It must be applied to every portion of the wound with a fearless hand, deep punctures having previously been laid open with the knife. In the absence of nitric acid, lunar caustic, the actual cautery, or strong antiseptics should be used. The importance of early and thorough cauterization cannot be overstated. There is strong experimental evidence that laying open the wound and the free use of nitric acid will save a certain proportion of cases even after a lapse of twenty-four hours. It should never be neglected, since it retards the development of the disease, and thus renders the Pasteur treatment more certain of effect.

**Pasteur Method of Immunization.**—Pasteur observed that by residence in the nervous system of certain species of animals the power of the virus was exalted, while, on the contrary, by residence in other species it became attenuated. By inoculation of rabbits in series, one from the other, we obtain a virus of greatly increased virulence, so that after about one hundred passages they will die with great regularity on the sixth or seventh day. Beyond this point no increase of virulence can be obtained, therefore, Pasteur gave it the name "fixed virus." On the other hand, when monkeys are inoculated in series, the period of incubation becomes gradually lengthened, until after a time the virus becomes so attenuated that it no longer causes death. This virus may be restored gradually to its original power by serial passages through rabbits or guinea-pigs. Thus Pasteur had at his command rabic virus of every degree of power, and in his early experiments he began his immunization with the greatly attenuated virus obtained from monkeys, passing gradually up from the weakest to the strongest produced in this animal, then passing on to the exalted virus in the spinal cords of rabbits in the same way, until the fixed virus was reached. At the end of the series he found his animals immune, not only against the fixed virus but also against the bites of rabid dogs. The method was not absolutely certain, and was, moreover, impracticable for obvious reasons.

With the assistance of Chamberland and Roux the method in universal use to-day was worked out, depending on the fact that the rabic virus contained in the spinal cords and brains of rabbits becomes attenuated fairly evenly and regularly by drying when protected from putrefaction, so that it is harmless at the end of fourteen or fifteen days. The method is carried out as follows: Rabbits are inoculated subdurally with the fixed virus daily.

At death, the spinal cord is removed with strict aseptic precautions, cut into three pieces, and suspended in large bottles containing a layer of caustic potash. These bottles have an opening near the bottom as well as at the top, both of which are plugged with cotton, so as to allow free passage of air. They are kept in a dark room at a constant temperature of 23° C. Thus, a full series of cords from fourteen days up to one day old is at hand, giving various attenuations of the virus from the weakest to the strongest. The usual dose is a portion of cord 2 to 3 mm. in length, which is prepared for injection by trituration and suspension in normal salt solution or bouillon.

After many experiments on dogs, during which it was proven that absolute protection could be given against the most powerful virus and also that the treatment was effective for animals even when instituted several days after infection, it was determined to try it on man. The first patient ever treated was Joseph Meister, an Alsatian boy of nine years, who was severely bitten on the arms and legs, July 4th, 1885. The worst wounds had been cauterized with carbolic acid after an interval of some twelve hours. Twelve injections were given in ten days, beginning with well-attenuated cords, and ending with a fresh cord which was fully virulent. Rabbits were inoculated daily with the same emulsions as the boy. Those inoculated during the first five days all escaped, while the remainder all died of rabies. The boy showed no signs of injury and five years after the treatment was in good health.

As practised to-day at the Pasteur Institute in Paris, the treatment is modified according to the urgency of the case. We have thus a "simple" treatment, lasting fifteen days, employed where the bites are slight; the ordinary treatment, extending over eighteen days, for cases of bites about the hand, limbs, etc.; and an "intensive" treatment, which requires twenty-one days, applied when the bites are about the face and head and a short incubation period is reasonably to be expected.

**Calmette's Modification.**—The method of preparing the vaccines as given above requires a large number of animals and much attention, and is too expensive unless the number of patients treated is very large, which is seldom the case. Calmette has introduced a modification which has been generally adopted in smaller institutes and found to be very successful. The requisite number of rabbits are inoculated with fixed virus every tenth day. The cords are removed at death, suspended over caustic potash, and placed in the drying chamber, as in the old method. After forty-eight hours, a portion of a cord is cut off and placed in sterile glycerine contained in glass-stoppered bottles. The operation is repeated each succeeding day until the fourteenth. It has been shown that cords so preserved retain their virulence unchanged for twenty-five to thirty days. In this manner the full series of vaccines is always on hand. Inoculations are begun with cord desiccated for fourteen days, and preserved twenty to twenty-five days in glycerine. During the last four days cords are used which have been in glycerine for five to ten days. The dose is a section of cord 3 to 5 mm. in length, made into an emulsion as described. Experiments by Cabot show that the virulence is preserved unchanged for a longer time when the glycerine is diluted. He advises that it be not stronger than one part to four of water.

**Dilution Method of Högyès.**—Pasteur believed that desiccation did not change the quality of the virus but brought about attenuation by diminishing

the quantity. Acting on this idea, Högyès, after many experiments, perfected a method of immunization by dilutions. He begins by injections of the cord of a rabbit killed with fixed virus, rubbed into a fine emulsion, and diluted with normal salt solution 1 to 10,000. Each day the degree of dilution is lessened, until at the end of the treatment it is only 1 to 100. His results, while good, are not as favorable as those obtained at the great majority of institutions where Pasteur's method is practised. It appears also from tests on animals that there is some danger of producing rabies, a risk which is absent from the method with dried cords.

The Pasteur treatment should always be begun as soon after the bite as possible. It is useless after the symptoms have declared themselves. The probabilities of failure are least in those who present themselves for treatment during the first week, since only those in whom the period of incubation will be less than twenty days will fail to receive immunity. The usual incubation exceeds this time considerably. It has been abundantly shown experimentally, as well as by comparative mortality tables, that the period of incubation is lengthened in persons who succumb after partial or complete treatment.

**Duration of Immunity.**—We have no statistics on this point for man. It has been studied in dogs, in whom the protection has been found to have disappeared in 21 per cent. at the end of one year, in 33 per cent. after two years, while in others it has persisted for five years. Persons bitten a second time by a rabid dog should again receive treatment, unless a very short time has elapsed.

**Serumtherapy.**—Babes and Lepp in 1889 reported experiments which showed that the blood of animals immunized against rabies acquired the power of more or less completely protecting other animals against the disease. In 1891 Babes and Cerchez reported further work, showing that the blood of a strongly immunized dog would in some cases entirely protect other dogs from experimental inoculation, while in those not protected it would greatly retard the development of symptoms. In rabbits it had no effect. They further showed that the virus was destroyed in vitro by the immune blood after six hours contact. Babes applied this method of treatment to 26 persons who were terribly bitten on the head by a rabid wolf. Twelve received the immune blood of men or dogs in doses of 10 grams, with 1 death. .

Tizzoni and Schwarz, and Tizzoni and Centanni, have prepared a serum which they believe to be both prophylactic and curative. They employ sheep as the producing animal, and begin their injections with emulsions of virulent nervous matter treated with gastric juice in order to attenuate it. After some twenty days the serum of the sheep has acquired such power that when injected twenty-four hours before inoculation with street virus it will protect rabbits in the proportion of 1 part of serum to 25,000 of body weight. In order to protect against fixed virus, however, the dose must be increased to 10 cc. for each kilo of body weight. In vitro, the serum destroys the virus in the proportion of 1 to 800 up to 1 to 1,600. In large doses it will protect rabbits against injections of street virus into the sciatic nerve, even after seven days. The vaccinal principle can be obtained from the serum in the form of powder by precipitation with alcohol and drying. Tizzoni and Centanni believe that treatment by their serum, or its active principle, is especially indicated in cases where it is necessary to produce

immunity rapidly, as in persons with severe bites about the face and head, or in those who have delayed treatment.

Marie, as the result of numerous experiments, finds that it requires a long period of vaccination against rabies to produce an active serum in mammals. The serum of non-vaccinated animals cannot neutralize fixed virus, but the serum of some birds possesses this power naturally.

At the present time it may be said that while the experimental results in the production of an antirabic serum are very encouraging, its use has not gained headway practically, the method of Pasteur still being almost universally employed.

**Prevention.**—Rabies is a preventable disease. Since more than 90 per cent. of all cases are due to bites from dogs, and since it is kept alive in the canine race, our measures must be directed to the control of these animals. It is better and more humane to have them under supervision than to subject them to the extreme measures sometimes enacted during the terror which reigns in a community in which an outbreak of rabies occurs. The wholesale destruction of dogs sometimes seen is cruel and wholly unnecessary. Among the measures proposed for the control of dogs may be mentioned high tax, muzzling, and the leash, with the destruction of homeless and wandering animals. The results of muzzling justify its recommendation, and there is little doubt that its strict enforcement will eradicate rabies from any community in a short time. Great Britain furnishes a striking example of its efficacy. In 1887 there were 217 cases of rabies in Great Britain; in 1888, 160; and in 1889, 312. The increase caused alarm, and muzzling was enforced, as a result of which, in 1890, 129 cases were seen; 1891, 79 cases; in 1892, 38 cases. There was much opposition to muzzling and the ordinance was relaxed. In 1893 the number of cases rose to 93; in 1894 to 248; and in 1895 to 672. Owing to the general alarm muzzling was again enforced, resulting at once in a marked decrease of cases, to 438 in 1896, 151 in 1897, 17 in 1898, 9 in 1899, and none in 1900.

## GLANDERS.

**Synonyms.**—Greek, malis; Latin, malleus, equinia; English, farcy; French, morve, farcin; German, Rotzkrankheit, Wurmkrankheit.

**Definition.**—Glanders is a specific contagious disease of solipedes caused by the *Bacillus mallei*, and transmissible to man by accidental inoculation. The disease assumes two forms, an internal, to which the name glanders is applied; and an external, which is known as farcy.

**History.**—As a disease of horses, glanders has been known for many centuries, the first systematic description of it being due to Vegetius Renatus, who recognized its contagious nature. Solleysel, 1664–82, taught both direct and indirect contagion, and established the relation between glanders and farcy. It was not until 1749 that the question of spontaneous origin was raised by the elder Lafosse, who held that glanders was an inflammatory, non-contagious disease. Although this view was combatted strongly by Bourgelat and Chabert, and the French governmental edicts of 1753 and 1784 held firmly to the doctrine of contagion, little by little the idea of Lafosse gained ground. Unfortunately the great veterinary school at Alfort went wrong, and as most of the army veterinarians were educated there, the

regulations against the disease were not enforced, and it became widespread. The school at Lyon always held to the doctrine of contagion, as did many well-known veterinarians in Germany, England and Italy. Waldinger of Vienna, in 1810, gave warning of the danger to man in dissecting the bodies of animals dead of glanders, stating that grave accidents and even death could result from infection through wounds. During the following year, Lorin, a French military surgeon, recognized glanders in man for the first time. In 1821, Schilling gave the first accurate description of acute gangrenous glanders in man, ascribing it to some poison from animals. He used the term "erysipelas" however. In discussing this case, Naumann, director of the Berlin veterinary school, and Holbach, stated that, while malignant inflammation and even gangrene sometimes followed injuries during the dissection of glandered horses, no instance of harm from living animals had been observed. Holbach expressed his willingness to inoculate himself with the material, so sure was he of its inoffensive character.

Instances of transmission to man multiplied, and, in 1822 and 1823, cases were reported in the *Edinburgh Medical and Surgical Journal*, which were proved by the inoculation of an ass. In 1829, Andrew Brown gave a most accurate description of a case, with autopsy. A year later followed Elliotsons'[1] notable paper, with reports of cases and autopsies. In 1837, the classic monograph of Rayer[2] appeared, which remains at the present day one of the most remarkable and best descriptions of the disease in man. The bacillus was discovered and cultivated by Loeffler and Schutz in 1882. Weichselbaum first isolated it from glanders in man in 1885.

**Glanders in the Horse.**—The disease assumes two types, glanders proper and farcy, though they may co-exist. In glanders the septum of the nose and neighboring tissues are chiefly affected. Nodules, which are firm and translucent gray in appearance, form in the mucous membrane, accompanied by inflammation and a catarrhal discharge. The nodules soften and break down, leaving irregular ulcers. The glands in the neck, mediastinum, etc., are usually involved. Nodules are always found in the lungs, with areas of congestion, and quite often in other organs. In farcy the disease affects chiefly the superficial lymph vessels and glands, which become irregularly thickened and hard, forming the so-called "farcy pipes" and "farcy buds." Softening and suppuration usually take place and ulceration follows. Secondary deposits often occur in the nasal mucous membrane and in the internal organs. Farcy is apt to run a more chronic course than glanders. The bacilli are found in the nasal discharge and in the suppurating lymph glands, and contagion is usually due to these discharges.

**Etiology.**—Glanders in man is almost always contracted from the horse, and is therefore practically confined to men whose occupation brings them into constant contact with horses, such as hostlers, drivers, farmers, veterinarians, knackers, etc. Wright has reported the case of a bologna sausage maker employed in a factory where worn-out horses were slaughtered. It has been contracted by drinking from the same bucket, or using a cloth with which the nose of a glandered horse had been cleansed. The disease is practically confined to men. In 120 cases, Bollinger found only 6 women.

[1] *Medico-Chirurgical Transactions*, vol. xvi, 1830; vol. xviii, 1833.
[2] *Mem. de l'Acad. Royale de Méd.*, Paris, 1837.

All affected tissues contain the bacillus, and are virulent; the discharge from the nostrils is perhaps the most frequent medium of contagion. The saliva is sometimes virulent from admixture with the nasal discharge. The blood rarely contains the bacillus and when present it is in small numbers. They pass into the urine not infrequently. Infection takes place most commonly through some abrasion. Mere deposit of matter containing the bacillus on the healthy skin is probably harmless. Guinea-pigs can often be infected through the skin by rubbing with a pomade containing virulent bacilli, but it is probable that the bacilli enter through minute and unseen abrasions. The bacillus probably penetrates the nasal mucous membrane quite readily. Small animals are easily infected by the simple deposit of virulent material in the nose. The conjunctiva is more resistant. Infection through the digestive tract takes place readily, the resulting lesions appearing first in the lungs, as a rule. Infection through the deeper respiratory tract appears to be rare. Glanders has proved very fatal to bacteriologists, a number of whom have lost their lives through accidental infection while studying the bacillus.

**Bacteriology.**—The bacillus was discovered by Loeffler and Schutz in 1882. It is quite irregular in form and size, being 2 to 5$\mu$ long, and 0.5 to 1$\mu$ thick. It stains readily, but not deeply, with the ordinary aniline dyes, and gives them up just as readily, hence it is difficult to stain in sections of tissue. It does not stain by Gram's method. It stains unevenly, presenting a beaded appearance. It is aërobic, non-motile, and does not form spores.

Growth takes place at 25° C. to 42° C., but best at body temperature. It grows readily on most of the ordinary culture media when once isolated. For isolation, blood serum and glycerinated potato are the best media. On agar and glycerine-agar it forms a grayish-white moist growth, which is viscid and tenacious. Bouillon is clouded uniformly, and a heavy slimy deposit is formed after several days. Later, a mycoderm may form on the surface. The growth on potato is specially characteristic. By the third day a yellowish honey-like growth is seen, which spreads and becomes darker, so that by the eighth day it is reddish-brown or chocolate-colored. The potato often shows a greenish-yellow staining about the edge. The organism is quite delicate. Cultures kept in the incubator usually die in two weeks. Kept at room temperature they live six to eight weeks. The bacillus soon loses its virulence in cultures, and must be passed through a susceptible animal in order to keep it up.

It is usually killed by drying in fourteen days. Exposure to light has a marked influence on it. The nasal discharge spread on filter paper is destroyed in eight days in the light, but survives twelve days in the dark. It resists putrefaction two to three weeks. The bacillus is destroyed by a temperature of 55° C. in ten minutes, and by 61° C. in one minute. A 5 per cent. solution of carbolic acid kills it in two to three minutes. Corrosive sublimate 1 to 5,000 destroys it in three minutes.

The presence of the bacillus in pus or the nasal discharge is generally determined by the intraperitoneal inoculation of male guinea-pigs. If it is present, in two to three days there is observed a marked swelling and redness of the testicles. Pure cultures are readily obtained from the testicles a few days later.

*Mallein* is an extract of the glanders bacillus containing the specific toxin, prepared by growing the organism for four to six weeks in 5 per cent. glycer-

ine bouillon. It is then sterilized, evaporated to one-tenth of the original volume, and filtered through porcelain to remove the bacilli. Before use it is diluted in a 1 per cent. solution of carbolic acid. When injected into glandered animals it provokes a definite febrile and local reaction.

**Morbid Anatomy.**—Glanders is usually classed among the infectious granulomata. Lesions may be found in almost every portion of the body. Superficially we find the various pustules, abscesses, and ulcers, with more or less extensive areas of erysipelatous and phlegmonous inflammation, all of which are apt to be about the face and limbs. These have the general appearance of the suppurative lesions common to different forms of pyæmia, and are especially characteristic of human glanders. The mucous membrane of the nose is covered with a viscous muco-pus, under which are found ecchymoses, pustules, and ulcers. The latter, especially in chronic cases, may expose the cartilages and bones, which are necrotic. The septum, vomer, and even the palate bones are at times necrosed. Cicatrices, which are frequent and extensive in the horse, are rarely found in man. Similar changes are found in the frontal sinus, the pharynx, larynx, and trachea. The joints frequently contain serous, sero-sanguinolent, or purulent fluid. Osteomyelitis and periostitis may be present, or there is more or less extensive necrosis of denuded bone. All of the internal organs may contain nodules. They are rarely absent from the lungs, though not apt to present the nodular character generally seen in the horse, in which animal the nodules have a strong connective tissue capsule, outside of which is a zone of cirrhotic lung tissue, in which the alveolar walls are very much thickened. They are scattered throughout the lung, but are most numerous under the pleura. They vary much in size. Wright regards the lesion as essentially a focal pneumonia, with suppuration and necrosis. Around the nodules are formed areas of œdema, hemorrhage and interalveolar fibrinous exudate. In chronic cases a capsule may be formed, as in the horse, and the central area becomes caseous, and, in the horse, even calcareous. The serous cavities often contain serum and blood.

The spleen is large, soft and filled with blood.

The liver shows fatty degeneration, and is the seat of metastatic abscesses.

**Symptoms.**—These vary with the form of the disease, which may be glanders or farcy, both of which may be acute or chronic. Acute glanders does not pass into the chronic type, but frequently the chronic form ends in an acute outbreak.

**Acute Glanders.**—The first symptoms may be chills, marked weakness, headache, anorexia, epistaxis, accompanied by more or less intense pains about the joints, which are more severe at night. As a rule, however, local symptoms appear before the general phenomena. The face, hands, and feet may become swollen and hard. The lymphatics become inflamed, forming hard cords, tender on pressure, and the corresponding glands grow large and painful. Phlebitis is sometimes observed. In fine, the early symptoms are those of pyæmia. After two or three days an erysipelatous condition appears about the face, and sometimes in the limbs or about the joints. The nose, lips, cheeks, forehead, and even the scalp, are swollen and discolored. Soon afterward a pustular eruption appears over these areas, somewhat resembling smallpox. The pustules are, however, pointed or flat, and not umbilicated. They are usually discreet, but may become confluent, forming purulent plaques. Bullæ containing sero-sanguinolent fluid are often

met with, which rupture, leaving foul ulcers, or else, by drying, crusts. Gangrene of the skin often occurs on the seat of these lesions, or follows the extravasation of blood into the cellular tissues. Under the gangrenous skin large collections of pus form, and, if life is prolonged sufficiently, the separation of the sphacelus may lay bare the tendons and even the bone.

In many cases, following the pains in the joints, hard tumors appear in the muscles on both sides of the body, which suppurate and discharge, often pointing beneath the bullous patches. With the cutaneous eruption the characteristic nasal symptoms appear, preceded by a sense of discomfort and obstruction in the nose and nasopharynx. Soon there appears an abundant muco-purulent, viscous discharge, often streaked with blood, which causes excoriations of the lip. Examination of the nose shows the mucous membrane to be red, excoriated, and often ulcerated. Pustules and ulcers may be found on the tonsils, pharynx, and larynx. The cervical and submaxillary glands enlarge, and sometimes suppurate.

As in the horse, a metastatic lobular pneumonia supervenes and hastens the end. Cough becomes harassing and dyspnœa marked. Impairment of resonance and rales are found, especially over the base of the lungs. The expectoration is muco-purulent.

The temperature is not much elevated at first; later it may reach 104° or 105° F. The morning remission is marked. The pulse is rapid and weak. There is often a fœtid diarrhœa. The urine contains albumin and sometimes blood.

The mind is sometimes clouded early in the disease, and a typhoid condition, with stupor, deafness, delirium or coma, may come on rapidly. Death may occur with coma or convulsions.

**Chronic Glanders.**—This form is met with usually as a sequence of chronic farcy, the nasal and respiratory symptoms coming on after a variable time, two to six months, though sometimes the type is chronic from the outset. Diagnosis is very difficult in these cases. The early symptoms are much the same as in the acute type, malaise, fatigue, pains in the muscles and joints. The mucous membrane of the nose and throat soon becomes involved. The nose becomes more or less occluded, and sometimes there is severe pain about the root of the nose, passing up toward the frontal sinuses. A muco-purulent discharge appears, often streaked with blood and containing crusts and small blood clots. Occasionally the discharge is abundant; again so slight that the nasal involvement may pass unobserved. Examination of the nose reveals ulcerations, sometimes exposing the bone, or even perforating the septum. Ulceration of the mouth, palate and larynx may also be found. The voice is altered and deglutition difficult. Cough is very annoying. Often there is pain along the trachea and behind the sternum, with tenderness on pressure. Involvement of the lungs is manifested by dyspnœa, frequent cough, with thick, grayish, blood-streaked sputum, profuse sweats, emaciation and exhaustion.

The other general symptoms are identical with those of chronic farcy—pains in the muscles and joints, neck and loins, diarrhœa, nausea, irregular chills and fever, sweats and progressive emaciation.

The course of the disease is slow, and remissions occur. Life may be prolonged for as much as six years, but cure seldom or never takes place.

**Acute Farcy.**—Acute farcy differs from acute glanders chiefly in the absence of involvement of the nasal mucous membrane. The general

symptoms are much the same, chills, headache, nausea and vomiting, with pains in the muscles and joints. The local symptoms are those of a poisoned wound. The point of inoculation becomes an unhealthy looking ulcer, the lymphatic vessels and glands become inflamed, tender and enlarged. The limbs become œdematous and erysipelatous. About the sixth or seventh day multiple abscesses begin to form in various parts of the body without relation to the point of infection. These may appear as inflammatory tumors, hard, tender, red or purplish in color, opening like furuncles, or as indolent, soft swellings with no reaction of the skin and surrounding tissues. They contain usually a sero-sanguinolent fluid, rarely pus, and result in the formation of ulcers. Besides these, large collections of pus form in the cellular tissues. The general condition of the patient is aggravated at the same time; there is marked fever and profound adynamia. About the third or fourth week a pustular eruption appears, which may be widely distributed over the face, limbs, and body. The eruption is often accompanied by gangrene. From this point, the symptoms are identical with those of acute glanders, though life is more prolonged. Delirium and coma supervene about the fifth or sixth week, sometimes in the third or fourth, and end in death.

**Chronic Farcy.**—Chronic farcy is more common than chronic glanders. The mode of onset is variable. Ordinarily it follows direct inoculation, with local manifestations of a poisoned wound; inflammation of the lymphatic vessels and glands appears in three or four days, accompanied with fever, nausea, and vomiting. In other cases the onset is very acute, with headache, nausea, high fever and delirium, these symptoms subsiding after three to four days. Again the onset is very insidious and slow. There are vague pains in the limbs and joints, with difficulty of motion. There is loss of strength and vigor without apparent cause. After four to six weeks, multiple abscesses form in the muscles or subcutaneous tissues, especially in the legs and about the joints. They are usually not painful and there is no marked reaction in the skin and surrounding tissues. The skin over them becomes purplish after a time. Their size is variable, some containing as much as 500 cc. of fluid, which may be blood, or blood and pus mixed. Laudable pus is rare. These collections may persist for six to eight months, opening externally finally, or sometimes being absorbed. Less frequently phlegmonous abscesses are met with, which form and open rapidly, discharging pus. The rupture of the abscesses leaves fistulæ which sometimes persist for a long time discharging an oily or gummy fluid, at other times healing rapidly. Successive crops of abscesses may follow each other for a long time, the patient becoming more or less emaciated and feeble.

The symptoms often abate and even disappear, so much so that cure may seem complete, but after a variable time, usually thirty to sixty days, relapse occurs and the disease resumes its course. Pains in the joints and various parts of the body come on, digestive disturbances appear, marked by nausea and sometimes vomiting. The abscesses for the most part now leave fistulæ or ulcers. Emaciation progresses rapidly, the skin becomes dry, hectic fever with chills and night sweats comes on. There is a persistent and fœtid diarrhœa. A dry cough is often present. The patient falls into a delirium which may end the scene. More often acute glanders supervenes, and rapidly terminates life.

**Diagnosis.**—This is difficult, except in acute cases where the history of inoculation is clear. The symptoms following inoculation resemble closely

those of any poisoned wound, the chief difference being that in glanders the period of incubation is usually three or four days, while in other forms, especially those due to streptococcus infection, the incubation rarely exceeds twenty-four hours. As soon as pus is formed, a bacteriological examination should be made. Glanders is best determined after the method of Strauss, by the intraperitoneal inoculation of male guinea-pigs.

In all cases the occupation of the patient should receive careful attention, though it is often very difficult to trace any exposure to a glandered animal.

The eruptive stage may resemble smallpox. The glanders pustules appear in successive crops and ulcerate rapidly. They are not umbilicated and not so uniform as variolous pustules. The chronic type may offer special difficulties. Certain types of syphilis closely resemble chronic glanders. Even the destructive changes about the nose are simulated. The differentiation may rest on the effect of specific treatment. In tuberculosis the lungs are generally the chief seat of the disease. The nose and skin are not usually affected.

**Serum Diagnosis.**—M'Fadyean has shown that the serum of glandered horses agglutinates the *Bacillus mallei* in dilutions as high as 1 to 1,600. The reaction is well marked in dilutions up to 1 to 1,000. Normal horse serum agglutinates slowly in dilutions up to 1 to 300. The cultures are grown in bouillon, and should not be more than two or three days old. His results have been confirmed by many observers.

**Prognosis.**—The outlook is bad in every form of glanders. Acute and chronic glanders and acute farcy are practically always fatal. Chronic farcy sometimes ends in recovery. The remissions which occur may mislead one. Hallopeau and Jeanselme have reported one case in which the remission persisted three years, new abscesses then appearing and the case resuming its course.

**Treatment.**—If seen early enough, the seat of inoculation should be laid open and thoroughly cauterized, preferably with the actual cautery. To be of value this should be done not longer than one hour after inoculation.

The treatment of the declared disease is local and general. Abscesses should be opened as they appear, evacuated and swabbed with a solution of chloride of zinc 1 to 10, or other strong antiseptic, then dressed with iodoform. Ulcers should receive the same treatment. Curettage has been advised before the application of the zinc. The nose may be washed out with permanganate of potash or boric acid solution, followed by insufflations of iodoform or aristol.

The general treatment is tonic and supportive. There is no specific or any drug that appears to have any special value. The best results seem to have been obtained from the use of sulphur and iodine in various forms. Bendall recommends benzoate of soda at frequent intervals. Nocard, M'Fadyean, and others, have conclusively demonstrated the curative effect of mallein in horses. Babes and Bonome have used it in chronic glanders in man in doses of $\frac{1}{15}$ to $\frac{1}{10}$ of a cubic centimeter, with apparently good results.

Great care must be taken with the discharges, soiled linen, etc., of patients, which should be destroyed as far as possible. Attendants should be warned of the danger from nasal discharge and the pus from the eruption, ulcers, and abscesses.

# CHAPTER IV.

## TETANUS.

By JAMES M. ANDERS, M. D., LL. D.

**Synonyms.**—Trismus; lockjaw; opisthotonos; German, Wundstarkrampf.

**Definition.**—Tetanus is an acute infectious disease caused by the toxic products of the tetanus bacillus. It is characterized clinically by painful muscular spasms, affecting first and principally the masseter muscles and those of the neck (*trismus*), and secondly, those of the trunk, especially the extensors of the spine and limbs (*opisthotonos*). The disease is endemic and rarely epidemic in large centres of population. Occasionally there are small epidemics, the origin of which can be definitely traced, as a rule. These have received various names according to the special circumstances under which they develop, giving rise to so-called vaccination tetanus (from the use of tetanized vaccine), diphtheria tetanus (due to the use of contaminated antitoxin), and tetanus neonatorum, occurring in new-born children, *e. g.*, where cases have developed in the service of the same midwife. Moreover, hospital epidemics have been known to follow the use of infected vaccine virus and cat-gut sutures.

The so-called idiopathic or "rheumatic" tetanus does not exist, as was formerly supposed, but, according to positive recent evidence, the disease is invariably traumatic in origin. This dictum receives striking confirmation from the results of a review of 1,201 cases by Anders and Morgan.[1] The incidence of the affection, as compared with the population, is gradually decreasing.

A distinction into acute and chronic forms has been made. The latter variety is commonly termed idiopathic or medical tetanus; it presents the same symptoms, however, as the acute or traumatic form, although less severe, and runs a longer course.

**Historical.**—In the writings of Hippocrates may be found brief and fairly accurate descriptions of tetanus. He recognized clearly that the disease is usually a sequel of wounds and fully appreciated its gravity. Among other ancient authors who described the affection were Galen, Celsus and Aretæus, but they distinguished the disease by the names of tetanus, opisthotonos, emprosthotonos and pleurosthotonos—appellations "expressive rather of the different inflexions of the body, than of any material variety with respect to the disease itself" (Cocke). Tetanus was not uncommonly confused with other diseases manifesting tonic muscular spasms, such as eclampsia, cerebrospinal meningitis, hysteria or hystero-epilepsy, and the like.

Galen maintained that the spinal marrow is the seat of morbid changes in tetanus—a view adopted by Fernelius, Hoffman, Willis, and other authors.

[1] *Journal of the American Medical Association*, July 29, 1905.

More recently, Sir Charles Bell and Magendie advanced the theory, based on experimental observations, that the tractus motorius is principally involved. As a natural sequel of this theory the belief gained currency, through the writings of Travers, Curling and others, that the disease is essentially of an inflammatory nature, although the term "irritation" was adopted to account for the nervous phenomena or so-called reflex convulsions.

To Aretæus we are indebted for a graphic description of the symptomatology and he also laments the physician's powerlessness to influence the fatal course. The writings of Maitre and Fragault furnish proof of its frequent occurrence after operations. In the military camps of the ancient wars it prevailed extensively, while in those of more modern times the disease showed a diminished prevalence. According to many of the earlier contributions, the disease would appear to be confined principally to tropical latitudes, but later opinion is, with justification, in more or less opposition to this view.

In more recent times are to be noted especially the writings of Larrey, Dupuytren, Laurent, Fernel, Verneuil, Curling, Romberg, Friedrich, and Billroth. The infectious nature of the disease was first recognized by Verneuil but it remained for Rose to advance our knowledge of tetanus to a notable extent and to prepare the way for the discovery of its bacteriological cause. Later, that philosophical observer, Nicolaier, demonstrated that pieces of infected earth the size of a pea would, when injected subcutaneously into the tail of a mouse, produce tetanus, while uninfected soil thus introduced into the animal failed to produce the disease.

**Etiology.—Bacteriology.**—In 1885, Nicolaier discovered the *Bacillus tetani*. It is a long, slender rod, one end of which is often occupied by a spore; this distends the cell into a pin or "drumstick" shape. The bacillus is 2 to 4$\mu$ in length and 0.3 to 0.5$\mu$ in thickness, but longer and thicker rods may be found in the cultures. It grows at ordinary temperatures, more rapidly still at the temperature of the body, and in milk, gelatine, and agar-agar; it is motile, is easily stained by Abbott's method, and is purely anaërobic. By means of Ehrlich's method, the fully developed spores may be stained. Kitasato was the first to make pure cultures; this is difficult since the presence of the smallest amount of oxygen interferes with their growth. The bacilli can be isolated from the wound in which they develop, but the tetanus bacilli do not enter the circulating blood and hence are not found in the various organs of the body. Neither do they grow upon superficial wounds as a rule, owing to their anaërobic nature.

If pure cultures are injected into animals, typical lockjaw ensues, but it would appear to be essential to lower the resistance of the infected locality in order to obtain the virulent effect of the organism. The bacillus produces a toxin, which, when inoculated, causes the lethal symptoms of the disease without the presence of the specific organism. Brieger has obtained two poisons from sterilized pure cultures, terming the one "tetanin" and the other "tetano-toxin," both being virulent poisons. It is to these alkaloidal substances that the tonic spasms are due, so that tetanus is classed as an intoxication.

*Mode of Action of the Toxins.*—According to Tiberti,[1] whose long series of experiments corroborate the work of Meyer and Ransom, the toxin passes

[1] *Centralblatt für Bakt. u. Parasit. Orig.*, 1905, Band xxxviii, p. 625.

to the nerve centres not by way of the lymphatics of the nerve, but through the plasma of the nerve fibers. It is necessary, however, that the axis cylinders preserve their normal integrity in order that the nerve fibers may take up the tetanus toxin and conduct it in the direction of the nerve centres of the spinal cord and thence "through the centripetal neuron to the muscles of the same region" (Babes). Direct inoculation of the spinal cord is followed by a brief incubation period and produces "tetanus dolorosus." The so-called local tetanus is brought about by subcutaneous injections of the toxins or inoculation of special nerves. Tiberti found that, following intravenous injections, all the muscles of the body are affected simultaneously, because the toxin is absorbed synchronously by all nerve endings.

*Bacillus Tetani Outside the Body.*—In the outer world the *Bacillus tetani* is found in many localities, most commonly in manure, garden soil, street-sweepings, and putrefying liquids. It is to be recollected that tetanus spores brought to a new locality may preserve their virulence for years; they may be contained in dust and carried into wounds and also into the respiratory and alimentary tracts, where they may set up their specific lesions in the presence of a diseased mucous membrane. Babes, in 2 cases of tetanus occurring in the human subject, found that inoculations with the fæces gave rise to the disease. MacFarland, from an analytical study of 95 cases of tetanus complicating vaccination wounds, concludes that the tetanus organism may be present in the vaccine virus in small numbers, being derived from manure and hay.

**Predisposing Causes.**—(1) *Traumatism.*—While it is undisputable that tetanus may be caused by any sort of wound or breach of the surface, in the investigations by Anders and Morgan, it was found that the preponderating proportion of cases occurred from severe contusions with penetration of foreign bodies. These researches also corroborate the generally accepted view that the most common sites of infection are the extremities, notably the hands and feet. Thus, in 863 cases in which the infection atria were noted, the arms and hands were the gateway for the poison in 294 and the legs and feet in 347 cases, the hands alone in 226 and the feet alone in 280. It was found to be frequent after gunshot wounds of the extremities and "Fourth of July hand injuries." Next to the extremities, comes cephalic tetanus with 58 cases. Finally, the figures indicate susceptibility of all parts of the body to the poison.

2. Geographical Location.—The disease is most common in tropical regions, although widely diffused throughout all civilized countries. The sections of the United States in which tetanus is most frequent are "northern New York, along the Hudson Valley, Brooklyn and the surrounding districts of Long Island, southern Pennsylvania, Virginia, Georgia at least about Savannah, southern Louisiana, Indiana, Illinois and southern California."

3. Seasons.—The incidence is decidedly influenced by the different seasons. In the statistics [illegible] cited above, the seasonal occurrence in 867 cases showed the following numerical order: July, 126 cases; October, 73; September, 66; June, 61; August, 56; May, 52; November, 47; April, 42; March, 41; December, 37; February, 31 and January, 33. The figures of July overbalance the great increase in July cases but, independently of this fact, the statement holds true that tetanus is more prevalent in the hotter as compared with the cooler months of the year.

4. *Age.*—It is generally believed that tetanus is most common between ten and thirty years of age, if we except tetanus neonatorum. The peculiar susceptibility of the new-born is due to wounds of the umbilical cord which serve as infection atria. The age in 583 of our cases showed between ten and fifteen years, 130, and between five and ten years, 99. From the fifth to the fifteenth years, 229 cases occurred (39.3 per cent.). Between the ages of fifteen and twenty-five years there were 145 cases (24.9 per cent.), while between twenty-five and thirty-five years, there were 86 cases (14.8 per cent.). Beyond fifty years there were only 14 cases.

5. *Sex.*—In 981 cases of the above series, there were 778 males and 203 females. The greater incidence in the male is readily explained by the more frequent occurrence of wounds.

6. So-called idiopathic tetanus is believed to follow exposure to cold or sleeping on the damp earth, but according to the most modern view there is in all cases a wound or injury of the skin or mucous surfaces, however trivial, which serves as a portal of entry. It has been contended that this explanation is scarcely admissible in accounting for the sudden appearance of the disease, as happens rarely a few hours after exposure to the cold, damp ground. The only tenable position, however, is to regard colds and catarrhal affections as favoring causes, and weakened conditions as increasing susceptibility.

**Special Pathology.**—There are few definite lesions and no constant changes in the brain or spinal cord. A careful postmortem examination often reveals small wounds, abrasions, or evidences of injuries or penetrating foreign bodies, most commonly in the hands and feet. Splinters are sometimes discovered under the nails. Various appearances are presented by the wound or injured part; it may show the presence of pus, collateral hyperæmia and more or less hemorrhagic extravasation. The nerves leading from the wound are often the seat of inflammation and the same is true of the umbilicus in cases of tetanus neonatorum.

In acute cases the density of the cerebral tissue is increased and the gray substance is distinctly hyperæmic. In the chronic form the brain and meninges are somewhat œdematous, and minute hemorrhages have been observed. Congestion of the nerve centres of the medulla and cord often resulting in inflammation and softening, especially in the territory of the anterior horns, is commonly noted. Perivascular exudations and granular changes in the nerve cells are among the histological changes.

**Immunity.**—Behring and Kitasato have produced artificial immunity in animals by the inoculation of cultures of the tetanus bacillus after the addition of iodine trichloride to diminish their strength.

**Symptoms.**—The duration of the period of incubation in human tetanus depends on the course, whether *acute* or *chronic*. In the acute form it ranges from a few days to two weeks, the usual period being from seven to nine days, while in the chronic, all the way from two weeks to months after the injury. There are exceptional instances in which the incubation period is less than twenty-four hours. In experimentally produced tetanus in animals (*e. g.*, in mice) the symptoms appear in from one to several days after inoculation with the specific bacillus and somewhat earlier still when the toxins are injected.

**Symptoms of Acute Tetanus.**—In a minority of the cases, mild prodromes, such as headache, pain in the back, languor and slight rigidity of

the extremities, are present for a short period, after which the characteristic manifestations develop either acutely or gradually. In many cases the patient quickly finds that he cannot open the mouth without great difficulty, and there is soon bilateral tonic spasm of the masseter muscles (*trismus*). More commonly, perhaps, the patient first complains of stiffness and tension in the muscles of the neck; this is followed, after a day at most, by spasm of the masseters, which renders the facial muscles immobile and locks the jaws (*lockjaw*). The rigidity of the muscles of the back of the neck is shown by the retraction of, and partially successful attempts at raising, the head. Rose points out that participation of the cervical muscles is evidenced by the fact that the patient can hardly touch the chest with his chin. In fully developed trismus the masseters are of stony hardness with palpable borders, and the physiognomy is often highly characteristic; it is immobile, the forehead commonly wrinkled, the eyes partly closed and drawn in, the corners of the mouth retracted, and the lips more or less protruded, producing a distinctive smile—*risus sardonicus*.

At this time the teeth are, as a rule, firmly clenched and a little later the muscles of the body become rigid; first the trunk (*orthotonos*), and then all the muscles of the entire back become affected, bowing the spine, the convexity presenting anteriorly (*opisthotonos*). After a couple of days the rigidity of the anterior abdominal muscles (especially of the recti) is observed, and their contractions may throw the body forward—*emprosthotonos*. Finally, nearly all of the voluntary muscles manifest tonic, preceded by clonic, contractions, although those of the arms usually escape. Curiously enough, in contrast with the upper extremities the legs show marked rigidity in extension. The patient assumes the lateral decubitus by preferance, as a rule, and maintains almost absolute quiet; he is readily disturbed.

Voluntary urination often becomes impossible owing to suppression or impediment caused by the muscular contractions, and the same is occasionally true of defecation. While the position of the body is one of continuous rigidity, from time to time exacerbating, convulsive seizures accompanied with most agonizing suffering, thoracic oppression, dyspnœa and more or less cyanosis (due to interference with the respiratory function), occur. The diaphragm may be similarly involved, causing sharp, lancinating pains at the base of the chest. In one patient, "convulsive dysphagia" (as in hydrophobia) was noted. These spasms are reflex in origin, although, according to Rose, in the advanced stage they cannot be produced voluntarily, and yet recur at frequent or infrequent intervals with great suddenness and severity. They can, however, usually be induced by slight external irritation, *e. g.*, by touching. All of the reflexes are decidedly exaggerated, but the sensorium remains unclouded.

Profuse sweating is commonly observed. Brown has reported a moderate leukocytosis (14,000 per cmm.). Leukocytosis as a symptom of tetanus has not received elaborate mention by writers; it is probably due to the suppuration in the vicinity of the wounds that serve as infection atria. The urine rarely shows traces of albumin and it has been demonstrated that the urea is not increased. According to Senator, neither creatin nor creatinin show an increase in the urine. Although at first sight a surprising fact, it is generally believed that tissue metabolism is practically unchanged in tetanus, the high and prolonged muscular tension notwithstanding. Fever of a moderate degree is generally present, although an afebrile course may be

pursued. Sudden and extreme exacerbations of fever to 110° or 112° F. occur and are pre-agonal as a rule. Hyperpyrexia, however, is not invariably fatal; it was present in 2 among the 1,201 cases analyzed by Anders and Morgan, both of which ended in recovery. These untoward elevations of temperature are probably due to paralysis of the heat-regulating centres. A postmortem rise of temperature may also be observed. The pulse is accelerated, but in the majority of instances only to a moderate extent. On the other hand, the pulse rate may be much quickened and at times a rapid increase to 148 to 180 is noted. Such a phenomenal rise is attended with arrhythmia and a marked falling away in force and volume of the pulse; it is ominous.

Although commonly fatal and always exceedingly grave, recovery is possible even in aggravated cases; a favorable course is indicated by a gradual diminution in the intensity and the greater infrequency of the spasms, while muscular rigidity also slowly disappears. The danger from exhaustion often followed by collapse of the circulation must be borne in mind. The writer saw one patient in whom apparently favorable relaxation of the tonic muscular rigidity was quickly followed by a fatal degree of heart failure. The principal causes of death are given by Cheyne and Burghard, as follows: (1) severe laryngeal spasm, terminating in fatal asphyxia; (2) spasm of the diaphragm or other respiratory muscles; (3) arrest of the heart's action, this may be due either to spasm or paralysis; (4) profound exhaustion and inanition, and (5) severe hyperpyrexia.

The *visceral complications* are few, but pneumonia and acute nephritis are occasionally observed. Inability to expectorate the bronchial secretion, as pointed out by Strümpel, may lead to the development of bronchitis or even of inhalation bronchopneumonia. Various accidents and rare clinical phenomena have been reported. The extreme violence of the tonic spasm may result in rupture of the muscles.

Of the series of 1,201 cases reviewed by Anders and Morgan, certain interesting features and complications were revealed. In 1 the trismus was so great that the teeth were crushed down to their roots. In 3 cases, in which no antitoxin was used, extensive desquamation of the skin, similar to that of scarlet fever, occurred. It is well understood that cases treated with antitoxin manifest erythema and urticaria with or without desquamation. In 3 cases the first symptom was severe pain in the region of the diaphragm. Fracture of the spinous processes of the vertebræ resulted from severe convulsions in 1 case. J. W. Ward reported to us a case in a man who had been bitten by a dog; the diagnosis of hydrophobia was maintained in this instance for several days. In 1 patient the pulse, following an operation, remained above 100 without discoverable cause until tetanus supervened. Another patient showed signs of irritability with unreasonable outbursts of anger, accompanied by jerky spasmodic movements, with a tendency to throw the head back, and nystagmus.

**Chronic Tetanus.**—The symptoms of trismus, or the first stage of the disease, develop less abruptly than in the acute form and are less pronounced. There are other cases in which the condition remains incompletely developed, the patient being able to separate the jaws sufficiently to allow of nourishment being given. In such cases the symptoms may suddenly become aggravated, soon to be followed, however, by a remission. In favorable cases the intervals of partial freedom from the painful tonic muscular spasms

grow longer and thus finally the stage of convalescence is reached. However, in certain cases the sequence is characterized by a gradual progressive intensification of the trismus and other symptoms, at last ending fatally. The cases that never become matured manifest slight if any constitutional disturbance, and not uncommonly terminate in recovery. Under these circumstances, the course of the affection may be greatly protracted. However mild a given case may be, the fact mentioned above, that it may suddenly manifest the severest symptoms, should be recollected more especially in connection with the question of the prophylactic treatment. Relapses are not uncommon unless the antitetanic serum is used.

**Head Tetanus.**—This is a special variety first discovered by E. Rose, and due to injuries, often trivial, confined to the distribution of the cranial nerves or more commonly of the facial nerve. This variety is uncommon, only 5 per cent. being due to face and head injuries. The most distinctive features are rigidity of the masseter muscles, and spasm of the pharynx and œsophagus, paralysis of the face on the side of the injury being usually associated. There are cases in which the spasmodic contractions of the œsophagus suggest a clinical analogy between the disease in question and hydrophobia. All other symptoms of ordinary tetanus are manifested in a more or less typical fashion, although the abdominal muscles are rarely involved. The great majority terminate fatally. Willard's statistics indicate that 25 per cent. of the chronic cases end in recovery, but in the acute form less than 10 per cent. survive.

**Tetanus Neonatorum.**—Tetanus in the new-born should be briefly described. The cases are divisible into two classes, *e. g.*, early and late, the former developing several days, and the latter eight or ten days, after birth. The most pronounced feature is trismus, which prevents both crying and the administration of food. Within a day or two opisthotonos supervenes and death soon follows. In the cases that develop late the violent muscular spasms occur at more frequent intervals; they rarely terminate favorably. The condition is often overlooked.

A collection of 1307 cases[1] from the United States showed the greatest prevalence in Louisiana, the District of Columbia, Maryland, Michigan, Illinois and Pennsylvania. In this connection it is of interest to note that the census report from Louisiana for 1870 and 1880 shows a total of 806 cases, of which 642 were instances of tetanus neonatorum. Happily the mortality figures show a marked decrease for the period between 1890 and 1900, as compared with the three previous decades.

**Sequelæ.**—The most common sequel is more or less muscular rigidity or stiffness, which may outlast tetanus for a period of months. Thus, in one patient of the series cited above, recovery ensued in eight weeks, but decided stiffness remained for eighteen months. In another, marked mental disturbance was noted for two months after recovery from tonic spasms, with perfect restoration at last. In another instance, acute nephritis followed the cessation of muscular contractions, and, later, suppuration of both parotid and the submaxillary glands occurred. Paralysis is a rare sequel; Kitasato has produced paralysis in man by the injection of small quantities of tetanus toxin into the femoral vein. Relapses are common; this is especially true of the trismus.

[1] Anders and Morgan: *Journal of the American Medical Association*, December 22, 1906.

**Diagnosis.**—The usual history and characteristic mode of invasion, especially the early appearance of trismus, followed by rigidity of the cervical and dorsal muscles, justify an assured diagnosis. There are, however, certain affections which bear a clinical resemblance to tetanus. Chief among these are cerebrospinal meningitis, hydrophobia, hysteria or hystero-epilepsy, tetany, and strychnine poisoning. In the subjoined table the distinguishing features of tetanus and strychnine poisoning are contrasted.

| Tetanus. | Strychnine Poisoning. |
|---|---|
| Reception of a wound, generally followed by a variable period of incubation. | Ingestion of strychnine, followed immediately by the symptoms. |
| Begins with lockjaw; then tonic spasm of muscles of neck; later spreads downward, the arms and hands escaping. | Begins with gastric disturbance or a tetanic contraction of the extremities. Hyperæsthesia of the retina occurs and objects look green. |
| Reflex spasms not present at the outset. | Violent convulsions present from the commencement. |
| Rigidity is persistent, except in the chronic form, in which partial relaxation may occur. | Intervals of complete relaxation. |
| The course is prolonged into days or weeks. | Course is brief, terminating speedily in death or recovery. |
| Cultures made from the discharges of the wound show the *Bacillus tetani*. | Chemical examination of the gastric contents shows strychnine. |

*Tetany* is distinguished by protracted spasms limited to the extremities (the hands in particular), and the laryngeal muscles, with complete intermissions; also by an increased electrical and mechanical excitability of the motor nerves and a characteristic posture. Moreover, it occurs chiefly in young subjects and there is no history of a wound.

In *hysteria* or *hystero-epilepsy* opisthotonos may be present but trismus is rarely observed, and, when fixation of the jaws occurs, the contractions of the muscles of mastication are manifested at irregular intervals. Hysteria also presents associated characteristic nervous phenomena and there is an absence of the history of a primary wound.

*Hydrophobia.*—This can be distinguished by a history of the bite of an animal, by the violence of the reflex spasms of the respiratory apparatus, the great intensity of the psychical disturbance, and the absence of trismus and opisthotonos. Cases of tetanus have been reported, although rarely, caused by the bite of an animal, *e. g.*, the dog. If in such instances laryngospasm and dysphagia arise, the resemblance to hydrophobia is close and somewhat puzzling, but the shorter period of incubation and the trismus and opisthotonos of tetanus would serve to eliminate hydrophobia.

*Cerebrospinal meningitis* shows rigidity of the cervical muscles and there may be opisthotonos, but true trismus does not occur. Again, the history and the associated clinical phenomena, such as vomiting, hyperæsthesia, herpes, and disturbances of the sensorium, suggest meningitis.

Certain cases of mild trismus will be found on careful investigation to be due to pharyngitis, tonsillitis, inflammation of the sphenomaxillary fossa or,

finally, arthritis of the temperomaxillary articulation. In all of these conditions, neither rigidity of the neck nor opisthotonos are present. On the other hand, they are at once shown to be non-tetanic, by the detection of their special cause. In doubtful cases, the main element, after excluding the commoner sources of tetanus infection, is a careful local inspection of the oral cavity, pharynx and the masseters both externally and internally. In tetanus, moreover, on passing the finger into the mouth of the patient, the acute edge of the rigid masseters is felt between the jaw and the zygomatic arch. Finally, the discharge from associated injuries should be examined bacteriologically for the *Bacillus tetani* in doubtful cases.

**Prognosis.**—In the majority of cases death ensues and the mortality is highest in those instances that arise after severe traumatism. The late-appearing cases, following an injury, give the most favorable prognosis. Anders and Morgan analyzed the incubation period of 858 cases with especial reference to the mortality rate. It was found that 194 (22.3 per cent.) showed an incubation of five days or less, with a mortality of 58.8 per cent.; 394 developed in from five to ten days with a mortality of 63 per cent.; 148 gave an incubation of from ten to fifteen days with a death-rate of 42 per cent.; and 98 cases developed in from fifteen to twenty-five days with a mortality of 40 per cent. Regarding the duration in 870 cases, it was observed that the highest death-rate occurred on the seventh days, or in 86 cases; the second day showed 71 deaths; the third, fourth and fifth days were rather constant, with about 50 deaths. From the tenth day gradually, and the fifteenth rapidly, the mortality progressively decreased. Again, of cases lasting five days or less, there were 338 with a mortality of 275, or 81.4 per cent.; in those giving a duration from five to ten days, or 231 cases, 144 deaths occurred, or 63 per cent.; and those lasting from ten to fifteen days, 91 cases with 27 deaths, or 30 per cent. Acute tetanus or that which developed within ten days gave a total of 568 cases and a mortality of 74 per cent. On the other hand, 211 cases lasted over fifteen days, with only 18 deaths, or 8.5 per cent. mortality.

Wilson,[1] in an analysis of 52 cases following vaccinia, found the incubation to be longer on the average and the mortality also somewhat higher than in the ordinary variety. With A. C. Morgan, the writer has collected 635 cases of which 615 died, 4 recovered, while in the remaining 16 the issue was not stated.

The early direct treatment of injuries has been effective in reducing the death-rate of this disease; its prevention by the use of antitetanic serum is also quite possible. Unfortunately, we have no drugs that exercise an unquestioned influence over the disease. Complications and accidents of a serious character are rare.

**Treatment.**—(1) **Prophylaxis.**—Certain measures of prevention are of first importance. The immediate radical cleaning of wounds, in which there is ground for suspecting that tetanus may develop, *e. g.*, those soiled with earth from gardens, punctured and lacerated wounds, is of the highest import. This embraces thorough disinfection and then cauterization. The cauterizing agents must be brought into contact with every part of the wound, hence, punctured wounds must first be laid open. Under certain circum-

[1] *Proceedings of the Philadelphia County Medical Society*, vol. xxiii, No. 1, pp. 149–165.

stances, excision of the wounds or even amputation is to be advised. The smallest foreign bodies (splinters) must be removed promptly. Friedrich recommends, in all wounds suggesting the possibility of tetanus, total excision of the focus and foreign body, supplemented by preventive injections of antitoxin. In the new-born the wound at the navel must receive the utmost care and attention to insure successful prophylaxis. According to Beumer, the infective agent may be conveyed by unclean hands or bandages as well as the raising of dust in the puerperal bed-chamber.

Many of the correspondents during the course of the collective investigations cited above, testified to the great efficiency of the dried serum used as a dusting powder after thorough excision and incision of the infected wounds. Prophylactic injections of antitetanic serum are undoubtedly effective and should be employed in all cases which call for wound purification. Not less than 500 antitoxic units should be administered for this purpose. Schreck reports his experience as follows: "In 1903 there were 56 cases of Fourth of July injuries treated, with 16 deaths from tetanus resulting; in 1904, 37 accident cases were given prophylactic injections of serum, with the result that no cases of tetanus developed."

Among other local measures may be mentioned carbolic acid, which, according to Baccelli, should be employed by subcutaneous injection. Other writers recommend that the suspected wound be sponged out with the undiluted acid. Again, the ice treatment of tetanus, which consists in immersing the part affected in ice with salt, or putting the patient in a very cold room, *e. g.*, a cold storage chamber, has been advised; this has been much employed in connection with the local use of the dried serum, with encouraging results, but is in the writer's opinion less effectual than the combined aseptic and antitoxin treatment.

2. **Treatment of the Attack.**—(*a*) The *general management* of the individual case is of considerable significance. The patient should occupy a quiet room from which the light has been in great part excluded. All possible sources of external irritation must be strictly avoided and a trained nurse should always be in charge.

(*b*) The *diet* should consist of nourishing liquids. The feeding should be systematic, the state of the patient being well considered. In those in whom the amount of food that can be administered by the mouth is insufficient, rectal feeding must be resorted to and nourishment may be introduced by means of a small soft stomach tube or catheter passed through the nares. Care is to be exercised to minimize the disturbance of the patient during the administration of food by these methods.

(*c*) *Stimulants.*—Although the painful tonic spasms of the muscles depend on a hyperexcitability of the motor tracts, cardiac stimulants should not be withheld when heart enfeeblement supervenes. Alcoholic stimulants are to be employed and the commencing dose should be one-half ounce of either whisky or brandy, to be increased if the effect be favorable in direct proportion to the urgency of the indications. Other stimulants may be administered in combination with alcohol. Of these, strychnine, camphor, and digitalis hypodermically are the most serviceable.

3. **Medicinal Treatment.**—Medicinal treatment has the double object of allaying the excitability and eliminating the toxins. The first indication is met by the employment of such drugs as opium, chloral hydrate, the bromides, calabar bean, chloroform by inhalation, cocaine, curare and the

like. In the writer's experience the spasms are best controlled by chloroform inhalations, keeping the patient somewhat under the influence of either morphine or chloral during the intervals. In view of the persistency of the muscular spasm, skillful care in the administration of the chloroform is absolutely necessary.

Opium or morphine is to be given with due caution in view of the fact that it exercises an inhibitory effect upon the respiratory centres, death in tetanus being usually by paralysis of respiration. Despite this theoretical objection, many authors regard this as the most serviceable remedy. Unfortunately, massive doses are required in many cases either to induce sleep or afford relief from painful muscular rigidity and convulsions. The best mode of administration is by hypodermic injection. As a hypnotic more may be claimed for the combined use of chloral hydrate and morphine than for the latter alone. The chloral may be given by enema, when there is inability to swallow, in doses of 4 gm. (gr. 60) every eighth hour, while the morphine may be used at the same time subcutaneously, the doses being large (gr. ss, gm. 0.03). The heroic administration of chloral is not unattended with danger and cardiac stimulants should be given during its employment.

According to the investigations of Morgan and the writer, the chloral-bromide treatment has been more generally employed, and the results obtained have been, on the whole, somewhat more encouraging than those from other methods. Calabar bean may be combined advantageously with opium or chloral, or employed separately. It has yielded satisfactory results but only in isolated cases. Cocaine has been injected under the spinal membranes, but has given only temporary relief from the convulsions. Babes speaks in favor of Bacilli's method, which consists of the subcutaneous injection of 5 to 10 cc. (℥ i to ij) of a one-half per cent. solution of carbolic acid along the spinal column, beginning at the neck, every two hours. According to this observer, however, Bacilli's treatment has been largely abandoned in Italy. Rarely, nitrate of amyl, physostigma, belladonna, cannabis indica, and curare have been found useful.

4. **Antitetanic Serum.**—The present view concerning the value of antitetanic serum is that, unless given before the appearance of the trismus, or before fixation of the toxins in the nerve cells takes place, it is of little, if any, utility. It should, therefore, be well understood that the responsibility of preventing the full development of this disease rests with the physician by the timely use of prophylactic injections of the antitetanic serum in cases where infection is probable.

MacFarland reviews a group of tetanus cases that occurred in the Philadelphia Hospital following vaccination. After 5 fatal cases had occurred, every suspicious vaccination wound was thoroughly excised and treated antiseptically. Notwithstanding these precautionary measures, "11 additional cases developed trismus and muscular rigidity, although after the administration of enormous doses of antitoxin they all recovered." Stintzing found that out of a total of 96 cases treated with Behring's serum, only 35 deaths ensued. Behring insists upon administering the serum within twenty-six hours after the onset of the attack. Again, massive doses as recommended by Copley (30 cc., to be repeated at least every six hours until improvement is noted) should be administered. When the antitetanic serum exerts a favorable influence, the spasms recur at longer intervals and with diminished intensity, improvement being gradual. Reports of cases in which Tizzoni's

dried antitoxin was employed internally were at first decidedly encouraging. The dose of the serum is 2.25 gm. at the first dose, and 0.6 gm. at subsequent doses. Roux and Borrel have found that intercerebral injections of antitoxin offer no decided advantages. The use of antitetanic serum has been followed by various results but appears to be without special therapeutic value in fully developed cases; it manifests its efficacy chiefly in cases of moderate gravity, but must be administered early.

# CHAPTER V.

## GONOCOCCUS INFECTIONS.

By RUFUS I. COLE, M.D.

**Introduction.**—The role which the gonococcus plays in human infections is now known to be an important one. The consideration of the local infections caused by gonococci in the genital tract does not belong here; but apart from these infections, gonococci not infrequently induce lesions in other parts of the body, either primarily, by extension, or by metastases. The following pages deal mainly with these extra-genital lesions, the great variety and gravity of which are astonishing. By the laity, gonorrhœa has been largely considered as a mild and, aside from the social aspects, unimportant disease. But the physician, who regards its far-reaching consequences, which are hardly secondary to those of syphilis, does not consider it so lightly. Considering the difficulty of cure of the lesions induced and the insidiousness with which the gonococcus acts, it is an adversary to be well reckoned with.

**Historical.**—Gonococcus infection is one of the oldest known diseases and is mentioned (probably) in the Bible. Up to the present century, however, it was confused with syphilis, being considered one of the manifestations of the latter disease. In the early part of the present century there were still two schools, the identists, who believed in the identity of all forms of venereal infection, and the unicists, who thought gonorrhœa and syphilis were distinct diseases. The former were supported by the well-known experiment of John Hunter, said to have been performed on himself, in which he inoculated gonorrhœal pus and syphilis resulted. Unfortunately for himself and the truth, he inoculated a mixed virus. But the unicists, under the leadership of Ricord, who recognized but one form of syphilitic infection, finally triumphed. It was not, however, until the discovery of the etiological agent of gonorrhœa that the identists were finally silenced.

While certain of the extra-genital manifestations of gonorrhœa, such as arthritis, were long ago thought to have an obscure association with that disease, it has only been in the past few years that the frequency and multiform nature of the extra-genital gonorrhœal infections have been made evident by the isolation of the infectious agent from these foci.

**Gonococcus.**—This organism was first described by Neisser (1879), who saw it in the purulent secretion from cases of urethritis and conjunctivitis neonatorum. Its specificity remained somewhat in doubt, however, until its growth in pure culture by Bumm in 1885.

The gonococcus, as it usually appears in pus, occurs in pairs, each individual having a form usually described as like a biscuit or coffee bean, the flat sides of the individuals being approximated. Such a pair usually measures in the long axis 0.8 to 1.6$\mu$ and in cross diameter 0.6 to 0.8$\mu$. As seen typically in gonorrhœal exudate, many of the pairs are found within leukocytes. In contradistinction to streptococci and staphylococci, these

organisms decolorize when stained by the Gram method. Lastly, they do not, under ordinary conditions, grow on the usual culture media, but require a medium containing uncoagulated albumin. The above points are the main differential ones. It must be insisted upon that morphology alone is not sufficient to distinguish this organism. Streptococci, especially when obtained from animal exudates, may occur in biscuit-shaped pairs. Most closely related, however, to gonococci are *Micrococcus meningitidis* and *Micrococcus catarrhalis*. In morphology and staining properties both of these resemble the gonococcus, but differ from the latter in growing on the ordinary culture media. While these organisms are not likely to cause errors in the study of urethral exudates, in the more unusual extra-genital lesions this possibility must always be borne in mind. On the other hand, gonococci in cultures do not always show the typical form mentioned above, but may appear in somewhat oval pairs, or as rounded individuals.

These organisms grow best on a culture medium composed of hydrocele fluid, one part, and nutrient agar-agar, two parts, or even better on a medium composed of human blood, one part, and agar-agar three parts. Up to the present time no animals except man have been shown to be truly susceptible to infection with the gonococcus.

The production of a toxin has been demonstrated by de Christmas, Wasserman and others. There is still a difference of opinion as to the exact nature of this toxin, whether it is an endotoxin and so only set free by the disintegration of the bacteria, or whether it is a toxin produced in media by the metabolism of the organisms. The part which this toxin plays in the production of infection is still undetermined.

## PRIMARY LESIONS CAUSED BY THE GONOCOCCUS.

The usual seat of infection by the gonococcus is one of the mucous membranes. Most frequently this is in the genital tract, the urethra in the male, the urethra or more rarely the vaginal or uterine mucosa in the female. Why there should be this special susceptibility of these tracts is entirely unknown. The infection of these membranes may be acute or it may have a very chronic course, urethritis lasting for months or even years with occasional exacerbations occurring not infrequently. Often the infection does not remain localized, but by direct extension the infection passes into the structures immediately surrounding the original seat. Prostatitis and epididymitis occur with great frequency in the male. The work of Wertheim and others has shown the great frequency with which inflammation of the tubes, ovaries and pelvic peritoneum occurs in women. It is these lesions especially which render this organism such a cause of misery in the human race. While all of these lesions are especially treated by the genito-urinary and gynecological specialist and are considered in books devoted to diseases of the genito-urinary tract, it must be remembered that these infections may be productive of the most obscure general manifestations. Young men are not infrequently treated for typhoid fever who are suffering from prostatitis, and women with pelvic peritonitis are treated for malaria and other infections.

It should be borne in mind that a most unusual train of symptoms may be associated with a chronic prostatitis. Aside from the neurasthenic features and indefinite pains, which so often are but a manifestation of this condition,

the patients may complain of abdominal pain, even of such severity as to suggest a renal calculus. Or the pain may be in the legs, like that of sciatica, or in the lumbar region, or the main symptom may be a severe pruritus ani. According to some writers, in one-half to three-fourths of all cases of gonorrhœa the prostate is involved, especially in the chronic cases, and by keeping this possibility in mind in cases presenting the above symptoms, the physician may by proper treatment relieve patients of these most distressing complaints.

The obscure symptoms associated with salpingitis and pelvic peritonitis in the female are better known.

Primary gonococcus infections occur not only in the genital tract, however, but they may occur elsewhere, and a knowledge of these latter infections is of the greatest importance. The other localities in which primary infections by the gonococcus have been demonstrated are the eye, the rectum, the mouth, the nose, and possibly in external wounds of the skin. As compared with the genital tract, however, all of these localities must be quite resistant to infection with this organism.

**Gonorrhœal Conjunctivitis.**—The association of purulent conjunctivitis with venereal disease was long recognized, but the absolute proof that it might be due to the same etiological agent as urethritis, was given only by the discovery by Neisser of gonococci in the purulent secretion from such inflamed eyes, and their cultivation by Bumm and Wertheim, and finally the experimental production of ophthalmia with pure cultures. These experimental inoculations were primarily undertaken for therapeutic purposes in cases of panus and of trachoma, as it had been noticed that a complicating conjunctivitis often had a decided beneficial effect in these conditions. The demonstration that the conjunctivitis of the new-born is due to this organism through infection from the mother during birth is of very great importance. Next to urethritis, conjunctivitis is the most frequent primary gonococcal lesion, and formerly its results were only slightly, if at all, inferior in importance to the genito-urinary lesions. The introduction by Crédé of the prophylactic use of silver nitrate in the eyes of the new-born, and so preventing this terrible disease, forms one of the most important and brilliant accomplishments of scientific medicine. Before this time, in the obstetrical institute in Leipzig, 10.8 per cent. of all new-born children suffered from conjunctivitis. Since then the frequency has diminished to 0.1 or 0.2 per cent. The great importance of this disease is shown by the fact that it is estimated that 10 per cent. of the cases of blindness in Europe are due directly to it.

**Conjunctivitis in the Adult.**—The healthy conjunctiva of the adult must possess a relative degree of immunity to infection with this organism, since, notwithstanding the very widespread distribution of urethritis and the frequent opportunities for the infectious material to be carried to the eye, cases of conjunctivitis in the adult are relatively rare. It must be borne in mind, however, that the opportunities for prolonged and severe infection of the eyes during childbirth are much greater than are at all likely to occur in adult life, and that also the natural protective mechanism of the eye in the adult is much more highly developed than in infancy.

The condition usually starts with great suddenness and intensity. Following the early signs of conjunctivitis, great swelling of the lids develops, the conjunctiva becomes roughened, and the secretion becomes purulent and frequently forms a grayish membrane upon the eyeball. Usually but one eye is affected at first, and the first care of the physician should be directed to

protecting the other one. This should be covered by a shield, the inner edge of which should be sealed with collodion, and every effort should be made to prevent the infective secretions gaining entrance to the healthy eye.

*Treatment.*—Cold compresses should be applied to the affected eye and very frequent irrigations with mild antiseptic solutions, such as boracic acid or potassium permanganate (1 to 5,000). After the great swelling has disappeared and the membrane is no longer present, 2 per cent. silver nitrate may be applied several times a day. It is of the greatest importance that physicians should not treat lightly any case of conjunctival infection where there can be any possibility of its being gonococcal in origin. The great danger is the involvement of the cornea and the formation of ulcers, leading to scar formation with resulting total blindness.

**Conjunctivitis Neonatorum.**—The onset is usually within three days after birth. The symptoms do not differ essentially from those occurring in the adult, except that in general the course is milder. The bulbar conjunctiva is usually not so seriously involved, and involvement of the cornea, while still frequent in improperly treated cases, is apparently less common than in adults.

*Treatment.*—The treatment is essentially that to be employed in adults. It is important to institute prophylactic measures in all new-born infants, both in private practice and in hospitals, whether the occurrence of gonorrhœa is suspected or not. The child should be bathed, without allowing the bath water to touch the eyes, and then into each eye a drop of 2 per cent. silver nitrate should be instilled. The objection to this application in all cases is that occasionally the silver causes a slight irritation lasting for several days. This has undoubtedly tended to prevent the universal application of this method, but, in the present light, physicians cannot neglect it without making themselves responsible in case infection supervenes. A commission appointed by the American Medical Association to investigate this subject, in the hope of inducing universal application of prophylactic measures, has decided to recommend the use of 1 per cent. silver nitrate solution, as being less irritating, and so overcoming any objections to its use, since experience has shown that a 1 per cent. solution is apparently as efficacious as stronger solutions. For further details in the prophylaxis and treatment of this condition the reader should consult the works on opthalmology.

**Gonorrhœal Proctitis.**—This condition is undoubtedly more common than is generally supposed. According to Baer,[1] infection of the rectum occurs in 30 per cent. of all cases of gonorrhœa in women, while Huber[2] places the number at 25 per cent. In 50 cases of vulvo-vaginitis infantum, Buschke found the rectum involved in 4, while Flügel demonstrated its involvement in 11 of 56 cases.

The mode of infection is usually, first, from the vaginal secretion, which is permitted to flow over the perineum into the rectum; second, from the use of soiled nozzles, rectal tubes or specula; third, by the rupture of an abscess into the rectum; or lastly, a result of abnormal coitus. The first mentioned mode is undoubtedly the most common one and explains the greater frequency of this form of infection in women.

[1] *Deutsche med. Wchnschr.*, 1896, vol. xxii, p. 116.
[2] *Arch. f. Dermat. u. Syph.*, 1897, vol. xl, p. 237.

There are two groups of cases of gonorrhœal proctitis; first, the acute, with severe pain in the region of the anus and with tenesmus, frequently associated with the formation of ulcers in the rectum, and second, a group of cases in which the symptoms are very mild, and to which the attention of the physician is frequently not drawn unless the condition be suspected and looked for. Cases of either the first or second group may run a prolonged course and lead to the formation of stricture. König has stated that gonorrhœa causes rectal stricture with greater frequency than syphilis.

**Treatment.**—In the acute stages the condition should be treated by irrigations of silver nitrate (1 to 4,000) or potassium permanganate (1 to 5,000). The sphincter should be dilated, and if ulcers are present these should be touched with the silver nitrate stick. Jadassohn[1] speaks of observing perirectal abscesses secondary to proctitis. In 2 cases in men such gonococcal abscesses were observed where the rectal mucous membrane appeared perfectly healthy.

**Gonorrhœal Stomatitis.**—While gonorrhœal infection of the rectum is usually recognized by its direct association with infection of the genitalia, the nature of such an infection of the mouth may be difficult to determine. The first definite proof that such a lesion may occur was given by the cultivation of gonococci from the diseased mucous membrane by Jesionek.[2] It is not sufficient for the demonstration of gonococci from this situation, that only morphology and staining reactions be considered, owing to the frequent occurrence in the mouth of *Micrococcus catarrhalis* and other organisms closely resembling gonococci. The mode of infection may be by the transference of infectious material on the fingers from the urethra or conjunctiva, or the mouth may be primarily infected by improper practices. In infants, in whom this form of infection is most common, the infection may occur from the mother during birth.

**Symptoms.**—The lesions usually consist of round, slightly elevated, gray-white spots scattered over the tongue and cheeks. They vary in size from that of a pinhead to that of a pea, or these smaller spots may be confluent over larger areas. There is no ulceration. The tongue is swollen, red and dry. Often the mucous membrane about the teeth is also swollen. The breath is foul. In some cases infection of the sublingual glands has occurred.

**Diagnosis.**—The diagnosis depends upon the history, the rapid course, the absence of ulceration, but above all on the cultivation of the organism directly from the lesions.

**Treatment.**—The treatment consists in antiseptic washes, careful cleansing of the mucous membranes of the gums and about the teeth, and in severe cases the application of silver nitrate.

Cases of infection of the nasal mucous membrane have been reported, but the clinical course has been atypical, and the bacteriological proof that such lesions are truly gonococcal is still lacking.

**Local Wound Infections.**—Following arthrotomy for gonococcus arthritis, infection of the incised wounds with gonococci may occur, as in 2 cases reported by Young,[3] and in at least one other seen by the writer. Baginsky and others have also reported such infection of the umbilical cord in infants. Juilliot has reported a case of gonococcal infection of the wound following

[1] *Deutsche Klinik*, Berl., 1905, vol. x, pp. 601-660.
[2] *Deutsches Arch. f. klin. Med.*, 1898, vol. lxi, p. 91.
[3] *Johns Hopkins Hospital Reports*, Baltimore, 1900, vol. ix, p. 677.

a radical operation for hernia, and F. Meyer[1] observed in a patient with vaginal gonorrhœa and multiple joint involvement, the gonorrhœal infection of a wound on the right middle finger. A panaritium developed and gonococci were found in the pus. Jadassohn states, that gonococci have been found in vesicles on the upper lip in association with stomatitis.

## GENERAL INFECTION CAUSED BY THE GONOCOCCUS.

It is now generally recognized that the local lesions at the portals of entry and in the adjacent structures are not the only ills attributable to the gonococcus. Evidence is rapidly accumulating to show that from these local lesions gonococci not very infrequently invade the blood. This is shown by the cases in which gonococci have been cultivated from the circulating blood as well as by the strong probable evidence shown in the cultivation of gonococci in foci far distant from the primary seat of infection, the probability being that the gonococci have been transported through the blood current, though of course this is not absolutely necessarily so.

Why in certain cases gonococci invade the blood and cause a septicæmia, or are carried to distant parts, setting up secondary infections, is not known. It was formerly thought that infection of the posterior urethra was always the preliminary event in a general infection. But it is now known that a general infection may be secondary to a conjunctivitis or other local primary infection. It has been considered by others that rheumatic and tuberculous affections, diabetes and alcoholism predispose to this occurrence. Others have considered that too active local treatment may give rise to a general infection. It was formerly thought that a too early stopping of the urethral discharge might be responsible for the occurrence of complications. Finger considers that in certain cases the bloodvessels of the prostate gland lie directly under the epithelium, and that these cases are more likely to have general infections than in cases where the bloodvessels are deeper. Pregnancy has been considered a favoring factor. Certain writers have considered that special races of gonococci are more likely to cause general infections, and in support of this quote cases in which husband and wife, or man and mistress, have infected one another, and both have developed metastatic lesions. None of these views, however, have much foundation on actual fact and the real conditions are still unknown.

**Gonococcus Septicæmia.**—The first probable demonstration of the invasion of the blood by gonococci was made by Wertheim, who, in sections made from an infected bladder, demonstrated the gonococci invading the small venules. The absolute proof, however, rested with the cultivation of these organisms from the circulating blood by Thayer and Blumer[2] in 1895. Since this time gonococci have been cultivated from the circulating blood in 5 other cases occurring in the Johns Hopkins Hospital, making 6 in all.

A review of the literature has enabled the writer to collect 29 cases in which there has been definite proof of gonococcus septicæmia by the isolation of the gonococcus from the blood during life. It is hardly possible to draw any sweeping conclusions from this small number of cases. In general they probably represent the more severe general infections, although some ran a

[1] *Deutsche med. Wchnschr.*, 1903, xxix, Ver. Beil. 226.
[2] *Bulletin of the Johns Hopkins Hospital*, 1896, vol. vii, p. 57.

comparatively mild course. Besides these well-authenticated instances, many others have been observed in which either from postmortem bacteriological examinations, or from the general features, the evidence is strong that a gonorrhœal septicæmia existed. This is especially true of the endocarditis and puerperal cases. Also, in most of the cases of local infection at points far distant from the portals of entry, we must suppose that the organisms have been carried through the circulation. In most of these, however, the number of organisms carried through the blood has been too few for us to speak of the condition as a septicæmia, or even as a bacteriæmia.

A study of the 29 septicæmia cases so far reported shows that they may be divided into four groups: 1. The cases in which endocarditis has been present. It is somewhat surprising to find that only 11 of the 29 cases belong to this group. In most of them the clinical features have been those of malignant endocarditis, with fever, sweating, chills, and frequently the association of septic infarcts. In 1 of them, however, there was only a mitral insufficiency of moderate grade, and this patient recovered. All but one of the remaining patients died.

2. The cases in which local suppurative lesions in the internal organs or in the subcutaneous tissue have occurred and the general features have been those of pyæmia. In this group belong 6 of the cases. Among the local lesions were subcutaneous abscesses, abscess of the prostate, suppurating inguinal buboes, suppurative seminal vesiculitis, epididymitis, parotitis, peritonitis, pleurisy and pneumonia. Of these, 3 died and 3 recovered, 2 of the latter after surgical intervention. In one occurring in the Johns Hopkins Hospital, the blood cultures were made 5 days after operation for peritonitis. Probably in this case the general infection occurred only secondarily as a terminal event.

3. Cases with no metastatic local infections, or only very mild and relatively insignificant ones. There were 10 of these; all of them recovered. Possibly, strictly speaking, most of these cases should be included in the former group, as the majority showed arthritis, some of them polyarthritis, but in most the joint involvement was mild; in some only joint pains were present. The only instance of strict gonococcus septicæmia, without any local foci whatever, occurred in the Johns Hopkins Hospital and is of great interest. In this patient, three months after an acute attack of gonorrhœa, there was a continuous fever lasting seven weeks, with headache, general malaise, an enlarged spleen and general features resembling typhoid fever. The Widal reaction was negative and cultures made from the blood showed the presence of gonococci. The patient made a perfect recovery and the absence of endocarditis is evidenced by the fact that there were no signs of any cardiac lesion five months after his discharge. This case shows that gonococci may cause a septicæmia of moderate grade, the general features of which are not unlike those of typhoid fever. It is possible that such cases occur with greater frequency than is now suspected, and this case may throw light on certain cases of continued fever which are now regarded as obscure.

4. Cases of gonorrhœal puerperal septicæmia. Two such cases have been reported, 1 of them from the Johns Hopkins Hospital. This latter instance was associated with malignant endocarditis. The other followed an infection of a perineal tear, with the development of a pelvic peritonitis, and later a general infection. Both of these patients died. The exact role which gono-

cocci play in puerperal fever is still unsettled. Some authors state that as many as 25 per cent. of all cases of puerperal fever are due to gonococci. This includes, however, the cases in which the infection is only a local one. The cases of general infection are probably much more numerous than the fact that there have been only 2 definite cases reported would indicate.

Taking the entire 29 cases, it is found that 12 died, 16 recovered, and the result in 1 was not stated. The prognosis, therefore, is not necessarily hopeless when gonococci are cultivated from the blood. The prognosis is worse when endocarditis is present.

**Method of Making Blood Cultures.**—In making cultures from the blood when gonococcus septicæmia is suspected, Harris has shown that it is not necessary that the blood be greatly diluted, as is the case with certain other infections, such as typhoid. The growth also occurs better on solid than in fluid media. An essential point is that the media contain a large amount of albuminous material, and this may be furnished by the blood itself. In making cultures it is advisable that at least 10 cc. of blood be obtained, under proper precautions, from one of the larger veins, in a sterile syringe, and this be added to melted agar in the proportion of 1 to 2 or 3, and that the mixture be then immediately poured into Petri dishes and allowed to solidify. Or the blood may simply be poured in a thin layer over the surface of slanted agar tubes or agar plates and allowed to clot. After from twenty-four to forty-eight hours the small colonies may be easily recognized. Owing to the susceptibility of the gonococcus to moderate heating, it is important that the temperature of the melted agar to which the blood is added be not above 40° C.

**Treatment.**—The treatment of gonococcus septicæmia does not differ from that of septicæmia due to other pyogenic agents. If local suppurative foci of infection be present, these should be treated surgically if they are accessible. At present there is no specific treatment for this form of infection. Possibly treatment by vaccines, controlled by the opsonic index, may be applicable in this form of infection, as it has been in other forms of septicæmia. The writer knows of no case in which this method has been tried.

## SECONDARY (METASTATIC) LESIONS CAUSED BY THE GONOCOCCUS.

Besides the cases showing secondary lesions in distant parts of the body in which the metastatic nature of the infection is rendered probable by the demonstration of gonococci in the circulating blood, there are other cases in which such definite proof is wanting, but yet in which the gonorrhœal nature of the local focus is shown by the cultivation of gonococci from it, or is rendered probable by the clinical association of the secondary focus with the primary lesion. There are several views as to the origin of these foci: first, that the infection is through the blood, second, that it is through the lymphatics, and lastly, that th lesions are due to toxins. There is practically no evidence at present that infection to distant parts of the body occurs through the lymph. We have lready stated that the role played by the toxins is largely hypothetical. The frequency with which gonococci are cultivated from extra-genital lesions seems to be directly proportional to the care with which they are looked for. Until the evidence with regard to toxins is more

convincing, it seems probable that these extra-genital lesions are due to the localization of bacteria in *loci minoris resistentiæ*, where they are able to set up lesions, even though the bacteria are in very small numbers. The possibility, however, that toxins alone may cause local lesions cannot be denied.

A word should be said here in regard to the treatment of all metastatic foci. While carrying out appropriate local treatment, the primary focus should not be overlooked. This is most often an acute urethritis or conjunctivitis, but not infrequently it is a chronic prostatitis or vesiculitis in the male, or salpingitis in the female. Obscure foci are too often entirely overlooked, with corresponding delay in resolution of the secondary lesions. It has been claimed by some that treatment of such primary foci may stir up the infection, cause increased re-inoculation, and so do more harm than good. There is little evidence for this, and the writer has never seen any harm come from proper treatment of the primary focus. Of course violent measures should be avoided as far as possible.

## GONOCOCCAL LESIONS OF THE HEART AND VESSELS.

1. **Endocarditis.**—The association of endocarditis with urethritis, and especially with gonorrhœal arthritis, was recognized as early as 1847 by Ricord, and later by Trousseau, Brandes and others. The proof, however, that the same etiological agent was concerned in the production of the endocarditis as in that of the urethritis was only furnished by the isolation of gonococci in pure culture from the circulating blood during life, and their demonstration in smears from the thrombus on the heart valve after death, by Thayer and Blumer[1] in 1895. Thayer and Lazear[2] observed a similar case in 1896, with cultivation of the gonococci from the circulating blood and also in pure culture from the vegetations on the heart valve after death. In the following year Lenhartz obtained the organism in pure culture from the heart valve, and demonstrated its specific nature by inoculation into the human urethra.

During the past ten years the number of cases in which the absolute bacteriological proof of the specific nature of the endocarditis has been furnished has grown large. In the Johns Hopkins Hospital alone 6 cases of endocarditis have occurred in which the gonococcal nature has been demonstrated by the cultivation of this organism from the blood during life, from the heart lesions at autopsy or by both methods.

Much doubt was at first expressed as to the possibility of the gonococcus alone setting up an endocarditis, and this was thought to be due to the ordinary pyogenic cocci which had invaded the body through the local venereal lesion. This view rested largely on the cultivation of streptococci by Weichselbaum and others from the endocarditic lesions in cases considered gonorrhœal. Further study has shown that there are probably two groups of cases:

1. Those in which the lesion is a true gonococcal one. To this the name "endocarditis gonorrhoica" has been given.

2. Cases in which there has been a mixed or secondary infection. To the cases of this group the term "endocarditis post gonorrhœam" or "endocarditis post gonorrhoica" has been applied.

[1] *Arch. de méd. expér. et d'anat. pathol.*, 1895, vol. vii, p. 701.
[2] *Medical Record*, New York, 1897, vol. lii, p. 497.

**Pathology.**—Little is known of the exact pathological changes present in the cases of simple endocarditis which usually recover and in which, therefore, no pathological study is possible. In the more severe cases in which the evidence as to the specific nature is more convincing, and in which there have now been frequent opportunities for postmortem study, the conditions are better known. These have shown the usual appearance of ulcerative endocarditis with polypoid thrombus formations. In many cases the extent of the latter has been enormous, with great fungoid masses extending from the surface of the valve, and by some this has been regarded as somewhat characteristic of this form of endocarditis. It may occur, however, in other forms, and is not infrequently seen in malignant streptococcus endocarditis.

As to the valves involved, it is of interest that in a considerable number of the cases in which the pure gonococcal nature was probable, the right heart was involved. In 15 cases collected by Thayer the following valves were affected:

| | | | |
|---|---|---|---|
| Left heart | aortic.... 7<br>mitral... 2<br>both..... 2 | Right side | tricuspid... 1<br>pulmonary. 2 |
| | 11 = 73.3 per cent. | | 3 = 20 per cent. |

Both sides, all four valves: 1 = 6.6 per cent.

Kulbs[1] has lately reported an additional instance and has collected all of the cases in the literature. He has included all in which there is evidence that the endocarditis was gonococcal, even though this is not always absolutely convincing. Of the 49 cases, 36 were in men and 12 in women. Involvement of the right side of the heart occurred in 10 cases, 20 per cent. Of the valves involved:

| | | | |
|---|---|---|---|
| Aortic in | 28 | Aortic and mitral in | 3 |
| Mitral in | 8 | Mitral and tricuspid in | 1 |
| Pulmonic in | 6 | Aortic, tricuspid and mitral in | 1 |
| Tricuspid in | 1 | All valves in | 1 |

The above statistics show the apparently greater frequency of involvement of the right heart in gonococcal than in simple endocarditis, even greater than that of other forms of ulcerative endocarditis, in which it is well known that in general there is a greater tendency to right-sided involvement than in simple endocarditis.

**Clinical Features.**—As in other forms of local gonococcal infection, males are more frequently affected than females, and young adults are most liable to the disease, though cases have been reported in children and in the aged.

There are two groups of cases showing clinical features corresponding to the anatomical lesions: (1) In one group the symptoms are those seen in other forms of simple endocarditis. It is difficult to be certain that these are truly gonococcal in nature, though the report by Prochaska of a case of simple mitral insufficiency with recovery, in which the organisms were obtained from the circulating blood during life, renders it quite probable that the cases reported as simple gonococcal endocarditis have been really such. It is quite possible that certain of the cases of chronic endocarditis

[1] *Wien. klin. Wchnschr.*, 1905, vol. xx, p 11.

in which no definite history of an acute infection can be obtained, originated from a mild urethritis. Further study along this line is desirable. (2) The symptoms in the cases of malignant endocarditis which have been carefully studied are essentially the same as those occurring in cases due to other pyogenic organisms. The fever is usually intermittent or remittent; chills and sweating occur frequently. There is usually a moderate leukocytosis and a rapidly progressive anæmia, at times as marked as that associated with general streptococcus infections. Arthritis is frequently associated with the endocarditis, though this is not invariable, and in many cases septic embolic infarcts may develop, or there may be involvement of the serous membranes, pericarditis, pleurisy or peritonitis. These two groups, however, are probably not sharply limited, and probably cases occur of all degrees of severity from the mildest to the most severe.

**Diagnosis.**—The diagnosis is made in the same way as in other forms of endocarditis. Its gonococcal nature may be rendered probable by the associated lesion at the portal of entry but the definite proof can only be obtained by the cultivation of the organism from the blood during life, which may frequently be accomplished without very great difficulty.

**Treatment.**—This does not differ from that of other forms of endocarditis. The considerable frequency with which this condition occurs should cause one to consider as suspicious all patients with urethritis having a continuous or irregular fever. In these the heart should be carefully and frequently examined, and, if there is any suspicion of cardiac involvement, the patient should be put to bed, an ice-bag placed over the heart, and the diet restricted. As in other forms of endocarditis, rest of the heart is probably the greatest factor in preventing advance of the process. As to the time which patients should be kept in bed after the acute stages are past, in the majority one may say as long as possible.

**Pericarditis.**—This occurs much less frequently than endocarditis, but may be present with endocarditis, as in the case of Thayer and Lazear, or in association with myocarditis, as in the case of Councilman. The writer knows of no cases of pericarditis without other cardiac involvement. The amount of exudate may be very slight, or, as in Councilman's case, very large, the pericardium containing at autopsy 800 cc. of a hemorrhagic exudate.

**Myocarditis.**—Changes in the myocardium of greater or less extent have been mentioned in association with most of the cases of endocarditis. Some have shown necrosis and embolic abscesses. Councilman has reported a case with severe hemorrhagic necrosis in the muscle wall in which gonococci could be demonstrated on cover-glasses. Another case of suppurative myocarditis has been reported by Iwanoff.

**Phlebitis.**—French writers especially have drawn attention to the occurrence of phlebitis in association with gonorrhœa. Heller[1] has been able to collect 25 such cases from the literature, besides 1 of his own. The pathogenesis of the condition is not certain. There have been no observations as yet to show whether the condition is due to the direct action of gonococci upon the wall of the vein, that is, whether it may be considered a specific gonococcus lesion, or only an associated phenomenon. Considering the great prevalence of gonorrhœa, one must be careful in attributing all lesions

[1] *Berl. klin. Wchnschr.*, 1904, vol. xli, p. 609.

which occur during the course of a urethritis to the gonococcus. The occurrence of phlebitis without any apparent cause and unassociated with gonorrhœal affections, to which Briggs[1] has drawn attention, must be kept in mind.

The writer has seen a case of spinal paraplegia associated with an acute gonorrhœa and complicated by incontinence of urine and cystitis. During the illness bilateral thrombosis of the femoral and probably the external iliac veins developed. The further course showed the spinal lesion to be of syphilitic rather than of gonococcal origin, and the venous thrombosis was probably due to an inflammation extending outward from the bladder; it may have been a specific gonococcus infection, but more likely was due to secondary invasion. However, the direct association with urethritis and the frequent association with other well-known complications of gonorrhœa, such as arthritis, in many of the reported cases make it extremely probable that the gonococcus alone may induce a true phlebitis. In 15 of the 26 cases collected by Heller arthritis also occurred.

The veins of the lower extremities are most likely to be involved, especially the internal saphenous. The clinical features do not differ from those of other forms of infectious phlebitis. Fever may or may not be present. Œdema follows the venous obstruction. In 16 out of 26 cases complete recovery resulted. In 1 of the cases gangrene resulted and amputation was necessary.

**Treatment.**—The treatment is the same as of other forms of phlebitis, wrapping the extremity in cotton, immobilization and elevation.

## GONOCOCCAL ARTHRITIS.

This is probably the most frequent and also the most important complication of gonorrhœa.

**Historical.**—The relation between arthritis and urethral inflammation was recognized by many of the older writers. The confusion which existed in the differentiation of syphilis and gonorrhœa, however, renders it difficult to determine whether they were describing the arthritis of syphilis or true gonorrhœal arthritis. Brande's[2] article in 1854 is the first clear discussion of the subject. Following this the condition was fully studied and its clinical features and association with gonorrhœa made clear. The proof, however, that the arthritis might be metastatic in origin and due directly to the presence of the gonococci rests upon the demonstration of these organisms in the joints. In 1883 Petrone described what were probably gonococci in microscopical preparations from the joints, but it was not until 1893 that Höch[3] succeeded in obtaining pure cultures and thus added the final proof.

**Etiology.**—At present two views are held as to the direct cause of the arthritis: first, that it is due to the action of soluble toxins elaborated at the seat of local infection; and second, that it is due to the localization in the joints of gonococci which have gained access to the general circulation, or have passed from the local lesions to the joints through the lymphatic channels. The main evidence in favor of the former view is that adduced

[1] *Johns Hopkins Hospital Bulletin*, Baltimore, 1905, vol. xvi, p. 228.
[2] *Arch. gén. de. méd.*, Paris, 1854, vol. ii, p. 257.
[3] *Wien. klin. Wchnschr.*, 1893, vol. vi, p. 736.

by Wassermann, who after injecting the toxin into his own body noticed pain in his limbs and joints, which lasted a couple of days. That, however, a true inflammatory reaction occurred in the joints is not stated. While possibly the action of toxins may explain some of the cases, the evidence in favor of this view is not very convincing.

On the other hand, the view that the lesion is due to the localization of gonococci in the joints is now well established by the cultivation of these organisms from the joints in a large number of the cases. It must be admitted, however, that from many of the infected joints no gonococci can be grown, even though the cultures are made with the greatest care. It is probable, however, that often the organisms are located in the tissues, even where the examination shows the exudate to be sterile. In a patient lately under observation, no bacteria, even with the greatest care, could be demonstrated in the fluid obtained by aspiration, yet smears made from a villus obtained from the joint, which was opened immediately after the aspiration, showed great numbers of gonococci. In 16 cases at the Johns Hopkins Hospital gonococci have been cultivated from the inflamed joints, while in 2 others gonococci were demonstrated on cover-slips, but could not be cultivated. In at least 13 other cases, however, no bacteria could be demonstrated on cover-slips or in cultures. As cultures were made, however, only from the more severe cases, it is probable that the above figures indicate a larger proportion of positive cases than can ordinarily be obtained by our present methods. Other observers have demonstrated their presence in a large proportion of the cases. In König's clinic, gonococci have been cultivated in one-third of the cases. Rindfleisch obtained positive results in 18 out of 30 joints examined. Weiss collected 121 cases from the literature in which a bacteriological examination of the joints was made. Of these, 92 were positive, but in only 21 were the organisms obtained in culture; in the remainder the evidence was obtained by microscopic examination alone. Baur obtained positive results in 19 out of 27 cases, by making cultures in Wassermann's nutrose-serum medium. He emphasized the importance of making the culture early in the disease, as in all of the positive cases the cultures were made before the sixth day, and in 8 of the positive cases second cultures made after the sixth day were negative. Moynihan was able to obtain positive results in 8 out of 27 cases.

Certain writers have laid great stress on the role which secondary and mixed infections play in the etiology. In the Johns Hopkins Hospital no other organisms have been cultivated from the joints and it is probable that other bacteria play little or no part in this affection.

That the organisms may persist in the joints after disappearance of the symptoms is shown by a patient, lately under the observation of the writer, who had been under treatment with vaccines for gonorrhœal arthritis of the right elbow, and was discharged on November 12th, the swelling having disappeared and the pain entirely gone. He went back to work, but continued to visit the hospital every few days for the purpose of having his opsonic index taken. On December 12th, he returned with lobar pneumonia. He entered the hospital and died from pneumonia on December 18th. Two days before death some swelling of the right elbow was noticed. At autopsy an acute and subacute inflammation of the elbow was found, from which gonococci were obtained in pure culture.

By what channels the gonococci reach the joints from the local lesions is in most cases not demonstrable of proof. In a few cases of arthritis the organisms have been cultivated from the circulating blood, but these have been the more severe cases usually associated with other features of septicæmia. It is altogether probable, however, that the path is through the blood current. The exact conditions under which the organisms leave the local lesion and are carried to distant parts are not known. There is much difference of opinion as to why the joints are seats of predilection for the secondary localization of these bacteria. The frequency with which slight injuries occur in the joints, so rendering them *loci minoris resistentiæ*, may be one factor, but it cannot be the only one. It must be remembered that in other forms of general infection, joint lesions occur not infrequently.

**Pathology.**—The surgical method of treating these inflamed joints has afforded opportunities for anatomical study of the more severe cases. König has made the following classification of the forms of gonorrhœal joint involvement:

I. Hydrops gonorrhoicus.
II. Arthritis sero-fibrinosa et catarrhalis.
III. Arthritis purulenta (empyema of joints).
IV. Arthritis phlegmonosa (essentially the peri- or para-articular form).

These forms, however, pass gradually one into the other and there is no sharply dividing line. The moderately severe cases which are most frequently seen at operation are not simple hydrops and yet have not reached the stage of empyema.

In joints of moderate severity which are frequently opened, there is quite marked œdema and infiltration of the peri-articular tissues. On opening the joint a large amount of turbid fluid escapes, which not infrequently contains large masses of fibrin. The synovial membrane is much injected and the villi are markedly swollen and red. Usually no erosion of the cartilage or bony change is present.

In the more severe forms the exudate is very purulent and marked erosion of the cartilage and even of the bone may occur. In the later stages, where there is marked limitation of movement, there is usually an extreme grade of thickening of the capsule and peri-articular tissues, but occasionally there is true bony ankylosis with marked thickening of the bones. The occurrence of osteophytes is rare but they are undoubtedly present in some cases.

The *x*-rays examination in the acute stages usually shows only the peri-articular swelling but no changes in the bones or cartilages. In the more severe cases the cartilaginous and bony erosions may be seen and later the thickening and ankylosis. Kienböck has pointed out that marked atrophy of the spongy portion of the bones occurs, as shown by the lessened intensity of the bone shadows. This, however, does not indicate any inflammatory process in the bones themselves and is not peculiar to gonorrhœal arthritis but occurs in all forms of joint infections.

**Frequency.**—Various writers estimate that from 2 to 5 per cent. of all patients with gonorrhœa suffer from this complication. It must be borne in mind, however, that many patients leave the genito-urinary clinic at the onset of arthritis and are treated in medical wards, that many infections are very mild and the patient or physician does not associate the joint trouble with the urethritis, and finally that many cases are wrongly diagnosed by the physician, so that probably the frequency is greater than that given above.

In 1905, 37 cases of arthritis diagnosed as gonorrhœal were admitted to the wards of the Johns Hopkins Hospital. During the same year 31 cases of acute rheumatic fever were admitted. Therefore, during the year, gonococcal arthritis was more frequent than acute articular rheumatism, and almost as common as tuberculous arthritis, of which there were 44 cases. König considers this the most frequent form of joint involvement, and states that "when a man has a purulent or sero-purulent joint inflammation, the urethra should always be examined, and in 90 out of 100 cases a tripper will be found."

Arthritis may follow any form of local infection with gonococci. As urethritis is by far the most frequent local gonococcal infection, arthritis is most frequently associated with this, but cases of arthritis complicating opthalmia neonatorum in infants or vaginitis in young girls are not at all rare. Arthritis following the inoculation of "tripper pus" into the eyes of trachoma patients for the cure of this condition, have been described.

**Age.**—As urethritis is most common during early adult life, gonorrhœal arthritis occurs most commonly during this period. No age, however, is exempt. It occurs in infants, secondary to opthalmia neonatorum.

**Sex.**—This complication occurs more frequently among men than women. Of 223 cases collected by Weiss, 117 were men, 76 women and 30 children. Of Northrup's 252 cases, 230 were men and only 22 women. Of 50 cases in the Johns Hopkins Hospital, but 7 were females. Possibly the greater frequency of genital gonorrhœa among men than women largely explains the difference, but it is probable that many cases in women are unrecognized. This is especially true of post-puerperal arthritis, many cases of which are gonococcal in origin. Begonin collected 42 cases of puerperal "rheumatism," and from their study concluded that they were gonorrhœal in nature; and the writer has lately seen a patient in whom the gonococcal nature of an arthritis following childbirth seemed very probable, if not absolutely definite.

**Race.**—Fourteen of the 50 Johns Hopkins Hospital cases were in the negro. The ratio of all colored to white patients in this hospital is 1 to 7. The greater prevalence of gonorrhœal arthritis in the colored is probably explained by the greater prevalence of venereal disease among them.

**Clinical Course.**—There are three forms of gonorrhœal arthritis; that seen by the genito-urinary specialist, that seen by the physician, and that seen by the surgeon. Every genito-urinary surgeon is familiar with patients who, during an attack of acute urethritis, complain of a little tenderness or pain in one or more joints. Little or nothing is to be discovered on examination of the joints, there is very little fever and in a few days the pains disappear. In a second group, or rather a second stage during which the physician is usually consulted, the joint pains are more severe, the joints are red, hot and swollen, there is fever, and the patient is often forced to go to bed. These are the cases which are so often mistakenly called acute articular rheumatism. There is a third stage, in which the brunt of the attack falls on one or two joints, or the earlier stages may be so slight and transient that the patient does not mention them in giving the history, and the whole picture is that of an acute suppurative arthritis. These are the patients who consult the surgeon, and it is for this reason that the picture of this malady is painted in such dark colors by many surgeons.

**Onset.**—The view is sometimes expressed that arthritis is more likely to occur during the course of a chronic gleet than during an acute urethritis.

This view does not receive support from our statistics, as in all but 9 of our 43 male cases, the arthritis followed the onset of acute urethritis in from one day to four months. In 23 of the cases, the arthritis occurred during a first attack of urethritis. The onset of the arthritis may follow the urethritis very quickly. In 1 patient the urethral discharge was noticed three days following exposure to venereal infection, and on the following day he had pains in the knees and ankles. A case has been described by Resnikow in which a sixteen year old girl developed urethritis and arthritis four days after marriage to a man suffering from gonorrhœa.

On the other hand, the arthritis may occur during a second, or even later attack of urethritis. Eleven of our patients gave a history of from one to four previous attacks of urethritis, and in 6 of these arthritis had occurred with the previous attacks of gonorrhœa. The view has been expressed that if arthritis occur during an acute urethritis, subsequent attacks are most likely to be accompanied by arthritis. There are not enough available statistics to enable us to decide this point.

In many other patients, on the other hand, no history of local infection can be obtained. This is especially true in women. In men there is usually a history of a past attack of urethritis; sometimes an unrecognized chronic gleet is present. Nine of our cases were not associated with acute urethritis, but in all but 4 there was a history of attacks one to ten years previously; and in all but 1 there were evidences of a chronic urethritis in the shape of "tripper-faden" in the urine or the presence of a urethral discharge containing gonococci.

The first symptom complained of is usually pain in the smaller joints of the hands and feet, though occasionally one of the larger joints, as the knee, may be involved from the beginning. The pain is frequently first noticed when the patient arises in the morning. Occasionally a history of exposure to cold and wet previous to the onset is obtained. This occurred in 7 out of our 50 cases. In this series a history of trauma was rare. Slight general malaise may occur for a few days before the onset, but the pain may occur with very great suddenness and without warning. In one instance the patient was perfectly comfortable, eating his dinner, when he was seized with a very severe pain in his hip, which so increased in intensity within a very few minutes that he was in agony and required morphia to relieve the very acute suffering. A chill may occasionally occur at onset and profuse sweating is not very uncommon.

**General Features.—Joint Involvement.**—Contrary to the usual statement, in almost all cases more than one joint is involved. In all but 3 of our 50 cases there was polyarthritis. On the other hand, the records in the surgical service of the Johns Hopkins Hospital show a considerable proportion of cases with monarticular involvement. Among 252 cases collected by Northrup, 56 were monarticular; of 348 cases collected by Jullien, 143 were monarticular. The probable reason for this discrepancy is that many are seen only in the later stages, when the disease is frequently localized in one or two of the larger joints, and the early history is not carefully considered. In many cases the early involvement of the small joints is slight, with few or no objective features. In other cases, however, a number of the joints show considerable swelling, redness and tenderness. The polyarticular involvement may last only for a few days, or a number of the joints may remain swollen during the entire course. Contrary to what occurs in

acute articular rheumatism, it is seldom that after recovery occurs in a joint it again becomes inflamed. All the joints are not necessarily involved at once, however. One joint may recover and others be involved in succession.

As to the relative frequency of involvement of the various joints, statistics differ, probably owing to the fact that frequently the milder infections are overlooked. The following table shows the relative frequency of involvement of the various joints. In column I are the statistics of 862 cases collected by Finger, Northrup, Weiss and Markheim. These figures probably include only the joints with fairly marked involvement. In column II, are the statistics of 50 cases from the Johns Hopkins Hospital. These include the joints showing marked involvement, as well as those in which the objective features were very slight or even entirely absent, the determination of joint inflammation resting entirely upon the patient's history. Lastly, for comparison in column III, the joint involvement in 310 cases of acute rheumatic fever, as given by McCrae from the Johns Hopkins Hospital, are quoted.[1]

| Joints Involved. | I. 862 cases. (Finger, Northrup, Weiss, Markheim.) | | II. 50 cases. (Johns Hopkins Hospital.) | | III. 310 cases. Acute rheumatic fever. (McCrae.) | |
|---|---|---|---|---|---|---|
| Knee | | 346 | | 75 | | 170 |
| Ankle | | 184 | | 49 | | 114 |
| Wrist | 87 | 111 | | 29 | | 83 |
| Carpo-metacarpal | 24 | | | | | |
| Shoulder | | 76 | | 20 | | 95 |
| Elbow | | 76 | | 16 | | 68 |
| Hip | | 59 | | 34 | | 66 |
| Small joints of foot | 61 | | | | 51 | |
| Metatarsal | 7 | 73 | | 35 | | 55 |
| Toes | 5 | | | | 4 | |
| Toes and heels | | 21 | | ... | | ... |
| Small joints of hands | 21 | | | | 53 | |
| Finger joints | 35 | 75 | | 13 | | 61 |
| Phalanges | 19 | | | | 8 | |
| Heel | | ... | | 7 | | ... |
| Sterno-clavicular | | 11 | | 7 | | 4 |
| Tempero-maxillary | | 26 | | 2 | | 0 |
| Sterno-costal | | 1 | | 1 | | 0 |
| Vertebral | | 5 | | 5 | | 3 |
| Sacro-iliac | | 5 | | 0 | | ... |
| Chondro-costal | | 2 | | ... | | ... |
| Pereneo-tibial | | 1 | | ... | | ... |
| Crico-arytenoid | | 2 | | ... | | ... |
| Scapulo-clavicular | | ... | | 1 | | ... |
| Symphysis pubis | | ... | | ... | | 1 |
| | | 1074 | | 294 | | 720 |

[1] These figures only include the joints acutely involved while the patient was in the hospital. If those involved before admission were added the number would be larger.

A study of these figures shows that the relative frequency of involvement of the various joints is about the same in gonorrhœal arthritis that it is in acute rheumatic fever, except in the case of the tempero-maxillary joint, which is not infrequently involved in gonorrhœal arthritis and with extreme rarity, if at all, in acute articular rheumatism. The most striking fact brought out by these figures, however, is that from the totals of columns I and III, one might conclude that the average number of joints involved in a case of acute articular rheumatism is almost 2½; while in gonorrhœal arthritis, the average number is only about 1¼. If we consider the figures in column II, which show the total number of joints involved, mild as well as severe, it is seen that the average number of joints involved in cases of gonorrhœal arthritis in the medical service of the Johns Hopkins Hospital is about 6, or over twice as many as in acute rheumatic fever. While larger statistics may show that this difference is not so marked, they nevertheless show what many have recognized for a long time, namely, that gonorrhœal arthritis in most cases is a polyarthritis, just as is acute rheumatic fever.

The affected joints are usually held quite firmly fixed. The pain and tenderness may be severe and constant but are usually markedly increased by motion. The pain may be partly due to the stretching of the capsule by the effusion, as in many cases aspiration markedly diminishes the pain. It may be severe, however, where the effusion is very slight. The effusion is usually most marked in the larger joints, especially the knee, in which case there is riding of the patella. But, no matter how large the effusion, one practically never sees the marked relaxation of the ligaments, with resulting dislocation and deformity, that sometimes occurs in the severe suppurative joints. The swelling is not always confined to the joint, but in the elbow may extend upward to the shoulder and downward almost to the wrist. Often on palpation points of especial tenderness are found. These are more often over the insertion of the tendons than directly over the bony prominences, as is seen in tuberculous arthritis. Frequently crepitus is obtained on passive motion, though this is not constant. Often the crepitus is due to involvement of the tendon sheaths.

Fluid aspirated from the affected joints may be quite clear or it may be distinctly purulent. Cytological examination of the fluid shows a preponderance of polymorphonuclear leukocytes. The fluid frequently has a slightly greenish tinge, a feature first pointed out by König. This is not characteristic of this form of arthritis, however; it may be present in acute rheumatic fever. The writer has seen brownish, probably blood-stained fluid aspirated from a joint which had not previously been aspirated. Generally the more severe the joint involvement, the more purulent is the exudate, though this is not an absolute rule.

**Fever.**—There is usually an irregular fever of moderate grade. In 50 cases the highest temperature was 103.5° F., but usually the temperature did not rise over 102°, in some not over 100° F. It is important to note that the fever may entirely disappear, while the local condition in the joint remains unchanged.

**Blood Changes.**—There is usually some anæmia, but not so marked as in acute rheumatic fever. In 19 cases the average number of red blood corpuscles was 4,685,000, and the lowest count 3,872,000. The average hæmoglobin estimation in 23 cases was 78 per cent., the lowest 50 per cent. A moderate grade of leukocytosis is the rule. In 38 cases the average count

was 11,500, the highest 20,200, and the lowest 5,000. In 23 of the cases the count was over 10,000. There is no apparent relationship between the degree of leukocytosis and the severity of the lesions.

**Diagnosis.**—In certain cases this is difficult. The conditions with which it is likely to be confounded are acute rheumatic fever, other forms of septic joints, tuberculosis, gout, and the acute stages of arthritis deformans. The writer has lately had under observation a patient in whom, following an acute urethritis, an arthritis appeared with a clinical course very like that of gonorrhœal arthritis. When the patient came under observation, only the right wrist was involved. The presence of tophi in the ears, however, led to some confusion, though neither the clinical course nor appearance of the joint suggested a gouty arthritis. Finally an *x*-ray examination showed a bony destruction and fusion much more like that seen in tuberculous joints than in gonococcal joints. The low opsonic index of the blood for gonococcus (0.5) suggested that the original diagnosis was the correct one, especially as no reaction occurred after the administration of tuberculin. In such cases, where aspiration cannot be performed and where the organisms cannot be cultivated directly from the joint, the correct diagnosis may be impossible and finally only be made with probability by the further clinical course.

The presence of urethritis, especially with the demonstration of gonococci in the discharge, is of great importance, although the possibility that the urethritis may be associated with some other form of arthritis must always be kept in mind. Entire failure to obtain relief of the pain by the use of salicylates is of considerable assistance in differentiating from acute rheumatic fever.

In the early stages the course does not aid materially. Certain of the smaller joints are not infrequently involved. The persistent involvement of one joint, however, especially if there be much effusion, is in favor of the condition being gonorrhœal. Involvement of the tempero-maxillary joint occurs more frequently in gonorrhœal arthritis. Sweating is often not so pronounced in gonorrhœal arthritis as in acute rheumatic fever, while cardiac involvement is more frequent in the latter. Examination of the blood gives little assistance. In doubtful cases, especially in the later stages, the *x*-ray examination is often of aid, especially in the differentiation from tuberculosis. In gonococcus infections of the joints the outline of the bones usually remains distinct, even though the cartilages are eroded, while in tuberculosis, the outline is often entirely gone and the bones appear as if fused. In gonococcus and other acute infections the atrophy of the bone is quite uniform, but in tuberculosis it is focal and irregular, and on the plate the bone appears mottled and "pitted."

The demonstration of gonococci in the fluid aspirated from the affected joint forms the only absolutely positive means of arriving at a diagnosis. In making cultures the fluid should be obtained by aspiration, the most rigid care in technique being employed. Cultures should be made by adding 3 cc. of hydrocele fluid to 10 cc. of melted agar and to this 1 cc. of the joint fluid is added and, after mixing, a plate is poured. Eight to ten such plates should be made and examined after twenty-four hours for the presence of minute colonies.

Meakins has lately studied the opsonic index to gonococcus in cases of gonorrhœal infections, especially arthritis, as well as in other forms of arthritis. In 26 cases of gonorrhœal infection, the index at the first examin-

ation (before giving vaccines) was, in all but 1, below 0.75, 1 being as low as 0.2. In the one exception, the index was 0.83, and in this case the diagnosis was doubtful. In 14 cases with non-gonorrhœal infection, the index ranged from 0.95 to 1. If this is constant, it is quite evident that it will be of considerable value in the diagnosis of the gonorrhœal metastatic infection. It is evident, however, that it will be of more negative than positive value, inasmuch as in many cases in which the exact nature of the lesion is doubtful, an acute urethritis is present, and this of itself would probably account for the low index. On the other hand, a normal or high index offers some evidence against the gonococcal nature of a joint affection. The variation in the index must be of sufficient extent that the possibility of technical error may be excluded. The absolute accuracy and value of this method of diagnosis is still uncertain.

**Treatment.**—In the mild attacks the main treatment should be directed to the genital lesion. Whether in these cases re-infection from the genital lesion is constantly occurring is not known, but there is little doubt that the patients recover more quickly when there is active and successful treatment of the primary lesion. The joints should also be protected from injury, and this is best accomplished by putting the patient to bed. Wrapping the infected joints in cotton, or the application of compresses soaked in a lead and opium solution often relieves the pain. In the acute stages the joints should be kept perfectly at rest, and this can best be done by fixation on splints. It is very doubtful whether drugs do any good. Many physicians employ potassium iodide, gr. 15 to 20, every four hours, with what are thought to be beneficial results. In a doubtful case it is well to try salicylates but if it be gonorrhœal arthritis, little result can be expected.

Rogers[1] has advised the use of an "antigonococcus" serum, which has been prepared by Torrey by the injection of cultures of the gonococcus into rabbits. The nature of the action of this serum has not yet been definitely determined and its value is uncertain.

Lately, the writer, in association with Meakins, has treated 15 patients with gonorrhœal arthritis by the injection of a gonococcus vaccine, controlling the dosage and time of administration by the determination of the opsonic index of the blood serum according to the method of Wright. The vaccine consists of an emulsion of gonococci in 0.85 per cent. salt solution. The number of bacteria per cubic centimeter is estimated by a special method, and the vaccine is then heated to 65° C. for one hour, to kill the organisms. The usual dose in starting is two hundred million bacteria, and this is repeated, or a larger dose is given, as the index, after the first rise, is falling. The attempt is made to keep the index as high as possible. A detailed report of these cases will be found in the *Johns Hopkins Hospital Bulletin*, 1907. The results so far have been encouraging, and sufficient to justify a more extensive application of the method. The main value has been in the more acute cases, though there has also been decided improvement in some of the more chronic ones. With this treatment, each patient must be carefully studied and followed, otherwise it is possible that the vaccines may do more harm than good.

Counterirritation, either by the application of the Paquelin cautery or by baking, seems frequently to have a beneficial influence. In using the oven,

[1] *Journal of the American Medical Association*, 1906, vol. xlvi, p. 261.

the joint should be wrapped in flannel, and the temperature raised to 250° to 300° F. for twenty minutes; then the oven is allowed to cool before removing the extremity. Of late years the method of producing passive hyperæmia, introduced by Bier, has been largely employed as a therapeutic measure with apparently good results. In applying this to the knee, a flannel bandage is first placed on the foot and lower leg. Then, a short distance above the knee, two or three turns of a thin, light rubber bandage are applied. This must not be tight enough to cause arterial obstruction. The toes should remain warm and the skin over the knee should become flushed and hot. If it is pale and cold, the tourniquet is too tight. If it causes pain it is too tight, and should be at once readjusted. It is advised to leave it on the first time not over three or four hours, but this time may be increased from day to day, so that after a few days the bandage remains on for twelve out of the twenty-four hours, or even longer.

Whenever the joint becomes distended with fluid this should be aspirated at once. This is a very easy procedure if the knee be affected, but more difficult in the case of the other joints. Very great care in technique should be employed in performing this operation. The removal of the fluid frequently gives great relief from pain, but often the fluid quickly re-accumulates. Repeated aspiration may be performed under these circumstances. The application of a tight flannel bandage immediately after may aid in preventing re-accumulation. The writer has had very little experience with the injection of iodoformized oil, dilute carbolic acid or solution of bichloride of mercury through a trocar. Guyot,[1] however, claims good results in 13 cases by washing out the joints, through a trocar, with bichloride of mercury solution 1 to 4,000. When such a procedure, however, is indicated, we feel that under circumstances where the surgical technique is good, it is better to perform arthrotomy and thoroughly irrigate the joint with one of the above solutions.

As soon as the most acute stages are over, passive motion should be begun and persisted in, despite the pain produced. In many joints showing firm fixation, this could have been prevented by the early application of passive motion and massage. Too much stress cannot be laid on this part of the treatment. It often requires considerable persistence on the part of the physician and much courage on the patient's part, but is frequently the only way to obtain a good functional result. Baking, massage, the Bier method and passive motion should all be employed during the later stages. There is no condition for which so much can be done by active treatment and none in which such deplorable results follow neglect.

**Surgical Treatment.**—The above described methods suffice in a considerable number of cases, but unfortunately, not in all, and in spite of the greatest care, some of the more severely affected joints will go on to erosion of the cartilage and bone with ankylosis, unless other measures are employed. It is to prevent this unfortunate result that recourse must frequently be had to surgical measures. Opening the joint and careful irrigation with antiseptic solutions will, in the majority of these cases, prevent the progress of the infection, and bring about rapid and complete recovery. The great difficulty is to make an early decision as to the joints which it is necessary to open. The demonstration of gonococci in the joint fluid has been considered by

[1] *Thése de Paris*, 1906.

some to be a positive indication for arthrotomy. Certainly where gonococci are found, it is much safer to call in a surgeon, but on account of the frequent difficulty in demonstrating the presence of gonococci in the joints, even when they are present in considerable numbers, we cannot rely on this criterion alone. On the other hand, we cannot state positively that every joint from which gonococci are cultivated will go on to suppuration and ankylosis. The writer has had one patient under observation in whom gonococci were cultivated from the joint fluid; the patient refused operation and the joint recovered completely with perfect motion.

Even though gonococci are not demonstrated, however, we feel that if on aspiration a very turbid cloudy fluid is obtained, and if the local and general symptoms are quite severe, the treatment should be surgical. Also, although the fluid obtained on aspiration be quite clear, if it repeatedly re-accumulates and the symptoms and signs remain marked, it is much safer to have the joint opened. It is impossible to give any absolute indications. Much must be left to the discretion of the physician in the individual case. It is frequently a difficult question, but it is better to err in occasionally opening a joint unnecessarily, than to allow one joint to become fixed and ankylosed. In coming to a conclusion, one is necessarily influenced by whether conditions permit perfect surgical technique or not. Of course this is absolutely essential, but with good surgeons and suitable surroundings, secondary infections should never occur; only a small incision, not over an inch long, need be made into the capsule. The joint should then be thoroughly irrigated with a solution of bichloride of mercury, 1 to 10,000, followed by normal salt solution.

Where ankylosis has already occurred, the treatment is most difficult. If the stiffness is due only to periarticular thickening, the adhesions may occasionally be broken up under a general anæsthetic, and by subsequent passive motion and massage a movable joint obtained. It may be necessary to repeat the movements under a general anæsthetic on one or more occasions. There is so much pain associated with this method, and it requires such a degree of Spartan fortitude on the part of the patient to keep up the motion in such a joint, that sometimes the result is hardly worth the effort, and it is extremely rare that a patient can be induced to persist sufficiently to obtain a satisfactory result. The method should always be tried, however. If bony ankylosis has occurred, the treatment must be entirely surgical.

**Results.**—With the methods outlined above, and especially with early operation in the more severe cases, the results are very satisfactory. The great danger is that permanent ankylosis may result, or that the condition may become chronic and a condition like arthritis deformans result.

**Relation to Arthritis Deformans.**—Permanent changes in the joints not infrequently follow the more severe cases of gonorrhœal arthritis. These changes may be associated with more or less persistent pain, and there may be mild exacerbations extending over considerable periods of time, even years. These features have led some writers to suggest a very close relationship between gonorrhœal arthritis and arthritis deformans, some even going so far as to suggest that gonococci may be the cause of certain cases of the latter disease. Stewart found a previous history of gonorrhœa in 30 per cent. of his cases of arthritis deformans. This, however, does not agree with the statistics of 110 cases reported by McCrae, in which this history was found only in 14 cases, or about 13 per cent. Goldthwait makes

a distinction on both pathological and clinical grounds between the cases of chronic arthritis following the acute infections, such as gonorrhœa, and true arthritis deformans. New bone formation may occur in the former, but the thickening is similar to that which follows a septic periostitis and occurs wherever the periosteum is present, and is not a thickening of bone at the edge of the cartilage, as is seen in true arthritis deformans.

Of special interest in this connection is the relation of gonorrhœal arthritis to so-called spondylitis deformans. In 1879 Bradford[1] described a case of ankylosis of the vertebræ following repeated attacks of gonorrhœal arthritis. König has described a similar case, and Heiligenthal[2] mentions cases reported by Bier, Marie, Raymond, Rendu and Renauld. The writer has seen several cases of spinal rigidity in which the onset was with arthritis associated with gonorrhœa. Whether anatomical and pathological differences in these cases will be found on further study remains to be seen. At present the whole question as to the relation of chronic gonorrhœal joint changes to arthritis deformans must be left open, until further work is done on the etiology and pathology of the latter disease.

**Painful Heel, Gonorrhœal Heel, Painful Foot, Talalgia.**—The exact relation of this affection to gonorrhœa has only lately been demonstrated. It was at first considered as an intercurrent affection in gonorrhœa, or a manifestation of a number of conditions, as gout, rheumatism, trauma, etc. Whether the same manifestations may occur in all these conditions or not is still uncertain, but it is now quite definite that the great majority of cases are gonorrhœal in origin. In 9 cases Vincent was able to show its direct association with gonorrhœa in 7, and of 10 cases reported by Durthe[3], 8 were undoubtedly gonorrhœal in origin. It occurs most frequently in men, especially in those actively engaged on their feet. The symptoms usually appear shortly following an attack of urethritis, or associated with it. Frequently with this arthritis occurs in one or more joints. It occurred alone in only 2 of Fournier's 11 cases, and only once in Durthe's 8 cases. In the early stages the patient complains of pain in the feet on walking. In the acute stages, the pain may not be localized, and the entire foot is sore and painful, with tender points over the tendons and small joints. When the patient consults a physician, the tenderness is usually localized to the plantar surface of the heel. The patient has a peculiar gait, in which most of the weight of the body is borne by the toes. Usually the pain is not present when the patient is at rest. The affection is almost always bilateral. There may be marked increase in the deep leg reflexes, even ankle clonus, and, as in a patient seen by the writer, the condition may at first suggest an organic lesion of the cord. The most troublesome feature is the chronicity. It often lasts for months, even for many years.

The nature of the underlying condition has been much discussed. In several cases in which operation was performed, French observers have found a bursitis. But tl is lesion has been found in very few of the cases and even then has not been very striking or definite. Others have found a fibrous thickening over the plantar surface of the calcaneum.

The important changes were first described by Jacquet in one of his cases. On the plantar surface of the heel, especially at the seat of origin of the

[1] *Boston Medical and Surgical Journal*, 1879, vol. ci, p. 698.
[2] *Centralbl. f. d. Grenzgeb. der Med. u. Chir.*, 1900, vol iii, p. 53.
[3] *Thése de Paris*, 1903.

flexor brevis digitorum muscle, was an exostosis. He thought this represented a late stage of the disease, which in the early stages consisted of changes in the osteofibrous structures over the plantar surface of the calcaneum, with subsequent bone formation, either a new deposit in the fibrous tissue, or a new outgrowth of bone. It was thought that this bony outgrowth rarely occurred, as it was only found in 1 case; and in 8 cases described by Durthe radiographs revealed its presence in only 1 case. Baer,[1] however, has lately described 6 cases, in all of which this exostosis was shown to be present by radioscopic examination. It is therefore probably not a rare form or stage of this affection, but occurs with considerable frequency. Five of these cases were operated upon and 4 were examined bacteriologically. In 3 of the cases gonococci were demonstrated, once in pure culture, and twice in stained sections, thus furnishing the absolute proof of the relationship of gonococci to this condition. He thinks, however, that other infectious processes may cause a similar condition.

Removal of the exostoses by incision on the lateral aspect of the foot has completely relieved these 5 patients, so that surgical interference is indicated in all patients showing exostoses.

**Gonococcal Bone Lesions.**—The acute bone lesions, as periostitis, osteitis and osteomyelitis have not been very carefully studied. Lately Watts has recorded a case of acute periostitis, with cultures of the gonococcus from the lesion. Osteomyelitis is of very rare occurrence. Undoubtedly all of these lesions may occur, but apparently the bony structures are not frequently attacked by this organism. These acute lesions have a more important surgical than medical interest and need not further be discussed here. In the discussion of the gonorrhœal heel, we have shown that true exostoses may be due to the gonococcus. Undoubtedly erosion of the ends of the bones in arthritis may afterward lead to new bone formation. Aside from the gonorrhœal heel, however, true exostoses are undoubtedly rare.

**Gonococcal Tenosynovitis.**—This is frequently associated with arthritis, but may occur independently. The infection usually occurs in the tendon sheaths about the ankle or wrist joints. Gonococci have been obtained from the exudate by Jundell, Bloodgood, Flexner and others. It is best treated by fixation and the application of the Paquelin cautery over the infected areas.

**Gonococcal Chondritis and Perichondritis.**—This is an exceedingly rare manifestation of gonococcal infection. In a case in an infant reported by Kimball,[2] an abscess of the larynx between the mucous membrane and the thyroid cartilages was found at autopsy. Cultures made from the pus showed a pure growth of *Diplococcus gonorrhoica*. A case has lately occurred in the Johns Hopkins Hospital, in which during an attack of gonorrhœal arthritis, tenderness and swelling developed over the thyroid cartilage. This patient made a perfect recovery. Finger has reported a case in which a pure culture of gonococci was obtained from an area of perichondritis about the cartilage of a rib.

**Gonococcal Myositis—Muscular Atrophy and Non-suppurative Myositis.**—Associated with arthritis in almost all cases, more or less extensive atrophy of the adjacent muscles occurs. This, as is well known, is not pecu-

[1] *Surgery, Gynecology and Obstetrics*, 1906, vol. ii, p. 168.
[2] *Medical Record*, vol. lxiv, p. 761, 1903.

liar to gonorrhœal arthritis, but occurs in association with all sorts of joint lesions. Whether this is an "atrophy of disuse" as it was formerly considered, or due to so-called "reflex trophic disturbances," or whether it results from direct extension of the inflammation from the joint to the surrounding muscles, probably varies in different cases. Kienböck and others have ascribed this atrophy in certain cases, where it is very extensive and associated with much pain, to neuritis, which they consider not infrequently associated with arthritis. In the cases like those of Dercum and Kienböck, where the atrophy is out of all proportion to the joint involvement, and where it progresses in spite of improvement in the joint condition, the atrophy is almost certainly due to a polyneuritis. Probably in some of the cases a true non-suppurative myositis occurs in association with the joint lesion. The differentiation of nerve and muscle involvement, however, especially when there is a great deal of peri-articular infiltration and œdema, offers very great difficulty, and it is questionable whether it can be done.

The occurrence of a non-suppurative gonorrhœal myositis unassociated with joint lesions has so far not been demonstrated.

**Suppurative Myositis.**—Acute inflammation of the muscles with pus formation may occur either as an extension from an infected joint or as a local manifestation of a general infection. The former probably occurs with considerable frequency, the latter with very great rarity (see Decousser, *Thèse de Paris*, 1905). Harris and Haskell[1] have reported a case of purulent myositis in which neither the history nor careful search at operation gave any indication of joint involvement. In this case the abscesses were in the gastrocnemius and soleus muscles and in the muscles over the sacrum. The treatment in these cases is surgical, free opening and drainage.

**Gonococcal Adenitis.**—Cases of adenitis with the isolation of gonococci from the infected gland have been reported by Pichevin and Raymond, Petit and others. The course is not characteristic and the treatment does not differ from that employed in other forms of suppurative metastatic infection of the glands.

## COMPLICATIONS INVOLVING THE NERVOUS SYSTEM.

Symptoms of involvement of the nervous system occur not infrequently in association with gonorrhœal infections. The etiological relationship is not clear, however. According to some writers, the lesions in the nervous system are due to the action of toxins, this view being based mainly on the experimental work of Moltschanoff.[2] This observer produced an ascending paralysis in animals by the injection of killed cultures of gonococci, and he was able to demonstrate definite microscopic lesions in the spinal cord and peripheral nerves. Many of the reported cases have undoubtedly been examples of purely accidental association of nervous lesions and gonorrhœa. The writer has seen an instance of spastic paraplegia associated with gonorrhœa, and at first it was thought that the lesion of the cord might be gonorrhœal in origin. On careful inquiry, however, a history of syphilis was obtained, and the nervous symptoms entirely disappeared under antisyphilitic treatment. A sufficient number of cases, however, have now been

[1] *Johns Hopkins Hospital Bulletin*, 1904, vol. xv, p. 395.
[2] *München med. Wchnschr.*, 1899, vol. xlvi, p. 1013.

reported to render it quite probable either that the gonorrhœal infection favors the development of certain nervous lesions which are not strictly gonorrhœal in origin, or that the gonococcus itself, or its toxins, may induce specific nerve lesions. So far, however, no specific clinical or pathological features have been noted.

The main lesions which have been described are the following:

**Neuritis and Neuralgia.**—During an attack of gonorrhœa there may occur either a *neuralgia* associated with paroxysmal attacks of pain in the course of the nerve trunks, or a *neuritis*, with more continuous pain, and tenderness over the nerves, with consecutive muscular atrophy and electrical reactions of degeneration. These forms of nerve involvement occur especially in association with inflammation of the adjacent joints. In many cases it is difficult to differentiate the symptoms of neuritis from those associated with the arthritis, especially where there is much muscular atrophy secondary to the joint involvement.

The nerves which are most frequently involved, aside from those associated with inflamed joints, are those in proximity to the genitals, especially the sacral trunks. In some of these cases, however, disease of the sacro-iliac joint may be present. Of Eulenberg's[1] 9 cases of neuritis, in 6 there was involvement of the sciatic nerve, in 2 of the tibialis, and in 1 of the radialis and medianus. All the cases of sciatica showed bilateral involvement.

**Sciatica.**—Lesser has drawn special attention to the gonorrhœal sciatica, and thinks that many of the cases of sciatica without obvious cause, especially in women, have this origin. He points out as distinguishing features the very sudden onset during or shortly after an attack of acute urethritis, the infrequency of recurrence except with a fresh attack of urethritis, and the presence of fever. Bernhardt[2] has reported a case of paralysis in the distribution of the musculo-cutaneous nerve, in which there was apparently no joint involvement whatever. Cases of optic neuritis and neuritis of the other cerebral nerves in association with gonorrhœa have been reported, but the nature of the association has not been made clear.

**Generalized Polyneuritis and Meningomyelitis.**—Cases of general neuritis unassociated with arthritis occur with very great rarity. Kienböck[3] was able to collect but 4 such cases. He regards these cases as toxic in origin. The association of lesions of the spinal cord with gonorrhœa has long been recognized. In 1803, Everard Hume reported a case of gonorrhœa with symptoms attributable to involvement of the spinal cord.

There have been several views held at various times as to the nature of the cord lesions occurring during gonorrhœa:

1. The early view that the symptoms are due to reflex impressions on the cord from the local lesion, the so-called "urinary paraplegia." There have been various modifications of this theory, but for none is there any evidence.

2. That a myelitis is present, originating by extension upward of a neuritis involving the nerves supplying the genito-urinary organs.

3. That a true meningomyelitis is present, due either to the gonorrhœal toxins or to a localization of gonococci in the cord. Leyden especially has drawn attention to the occurrence of gonorrhœal myelitis. In 1894, Barrie

[1] *Deutsche med. Wchnschr.*, 1900, vol. xxvi. p. 686.
[2] *Berl. klin. Wchnschr.*, 1905, vol. xlii, p. 1097.
[3] *Saml. klin. Vortr.*, Leipz., 1901, No. 315.

collected 25 of these cases; in only a very few, however, was the clinical diagnosis confirmed by postmortem examination. In the only case with positive bacteriological findings, staphylococci were cultivated. The whole question requires further elucidation, and the matter can only be settled by the further study of cases with modern methods.

**Neuroses.**—Of more importance probably than the organic gonorrhœal nervous lesions, is the functional psychic disturbance which so often accompanies and follows the gonococcus infection, especially when this is prolonged and associated with metastatic foci. While properly not strictly part of the gonorrhœal infection, it belongs to the so-called "paragonorrhœal complications" (Jadassohn); namely, these processes in which neither the gonococcus nor its toxin may be regarded as the direct cause of the phenomena. The symptoms may be of any grade, from slight mental depression and psychoneurosis to hysteria, psychasthenia or marked melancholia. These symptoms are not infrequently seen in patients with arthritis and form a distressing feature of this condition. They are especially marked in chronic prostatitis. In some cases, with the relief of the prostatic irritation, the mental features entirely disappear. It must be remembered, however, that the local treatment has a marked suggestive influence, and it may be difficult to determine whether it has been the psychic or organic treatment which produced the desired result. In many cases with prolonged pain, as in arthritis, the patients are conscious of a constant feeling of self-reproach, and unless they are skillfully treated and encouraged, the neurosis may become of more serious import than the gonorrhœal infection itself.

## PULMONARY COMPLICATIONS.

**Pneumonia.**—Either lobar or lobular pneumonia may occur during an attack of gonorrhœa, and pneumonia has been present in certain cases of gonorrhœal septicæmia. The pneumonia occurring under these conditions, however, shows no special features, and the absolute proof is still wanting that gonococci play a direct role in the production of this lesion. The finding of gonococci in the sputum of these cases must be accepted with caution, unless care has been taken to exclude *Micrococcus catarrhalis*. In a case reported by Bressel,[1] of a young man with acute and severe gonococcal urethritis, who had lobar pneumonia, Gram negative diplococci were not only demonstrated in the sputum—only on microscopic examination, however—but typical gonococci were cultivated from the circulating blood. While this cannot be considered absolute proof that the pulmonary lesion itself was due to gonococci, yet it renders such probable. This patient recovered.

Pulmonary infarction has occurred in cases of gonorrhœal endocarditis (case of Thayer and Lazear).

**Pleurisy.**—A considerable number of cases of pleurisy said to be due to gonococci have been reported. In most of these the proof is lacking. The demonstration of the etiological agent in the pleural effusion in so many cases of pleurisy, especially the tuberculous form, is attended with so much difficulty that negative cultural results are very little evidence that a pleurisy is gonococcal in origin. Also in pleurisy due to the pneumococcus, the organisms in the fluid often show degenerative forms and stain poorly and

[1] *München. med. Wchnschr.*, 1903, vol. 1, p. 562.

resemble gonococci, so that little reliance can be placed on the microscopic study alone of the pleural exudate. There seem to be only 3 cases in which the proof seems fairly good, by the demonstration of gonococci in both cultures and cover-slips, that the pleurisy was due to this organism. These are the cases of Chiaiso and Isnardi, Mazza, and Cardile. These were all in females, 2 of them in young girls. In 2 arthritis was also present. In 1 case the pleurisy was bilateral; all were with effusion. In all the course was prolonged. All recovered. From the few cases it is impossible to give any accurate clinical picture of the condition.

## RENAL COMPLICATIONS.

**Albuminuria.**—Albuminuria frequently occurs during the course of gonorrhœa. As Lewek has shown from a study of 155 cases, the albuminuria is usually associated with the presence of blood and pus, and has no significance as to the presence of a renal lesion. In the few cases where the amount is too large to be accounted for in this way, it may be due to a febrile albuminuria, the fever being due to the other complications usually present in such cases, or the albuminuria may be associated with irritation of the kidneys by administered drugs, such as sandal-wood oil or copaiba. In none of Lewek's 155 cases was a kidney lesion present. There is no evidence that the gonococcus or its toxin plays any role in the production of an acute or chronic non-suppurative nephritis.

On the other hand, it is undoubtedly true that suppurative kidney lesions may be due to the gonococcus, either as a result of ascending infection from a cystitis, or as a focus of infection in pyæmia. The proof of this rests largely on the work of Young. In a patient with all the features of a bilateral pyonephrosis, gonococci in pure culture were obtained from the urine. This seemed to be a case of ascending infection. In a case of Berg's, of fatal gonorrhœal endocarditis, a mild grade of pyelonephritis was present, apparently due to the gonococcus. The reported cases of pyelitis, pyelonephritis and pyonephrosis coming on during acute gonorrhœa are not uncommon. The actual demonstration that these are true cases of gonorrhœal infection of the kidney, however, has usually not been forthcoming. Certain of these cases, as Young's, have had a very chronic course, but the clinical features have not yet been well enough studied to differentiate conditions due to gonococci from those due to the ordinary pus organisms.

**Cystitis.**—That gonococci alone may induce an acute cystitis has been shown by the work of Young,[1] who from such a case obtained a pure culture of gonococci in the urine by suprapubic aspiration of the bladder. That gonococci, however, may be present in the bladder without inducing a cystitis has also been shown by Young. A second factor therefore must occur in the etiology. Young has also reported a case of chronic cystitis, in which this organism was shown to be the sole bacterium present.

## GONORRHŒAL PERITONITIS.

That a local circumscribed peritonitis may be caused by the gonococcus alone was definitely established by Wertheim in 1891, so overthrowing the

[1] Young: *Johns Hopkins Hospital Reports*, vol. ix, p. 677.

view previously held that the peritoneum possesses an immunity to infection with this organism. This local peritonitis is usually associated with salpingitis, and has mainly a gynecological interest.

Pelvic peritonitis occurs also in the male and Battez[1] has collected 30 cases. It is almost always secondary to gonorrhœal cystitis, prostatitis, or especially epididymitis and vesiculitis. There is usually intense pain in the inguinoscrotal region radiating to the iliac fossa. It has a short duration, intense local and general symptoms, and a relatively favorable prognosis. Rectal examination is of the greatest value for diagnosis.

The occurrence of a pure gonorrhœal general peritonitis, while long suspected, was only definitely established by the demonstration, by Young, of gonococci in pure culture in a case of general peritonitis occurring in the Johns Hopkins Hospital in 1898.[2] Up to the present, 9 cases of general gonococcus peritonitis have occurred in the wards of the Johns Hopkins Hospital. These have been collected and the subject discussed by Hunner and Harris,[3] who were able to collect 18 cases in which there was absolute bacteriological proof as to the nature of the condition, and 21 cases in addition in which there was good clinical evidence. That within a period of four years, 9 cases should have been treated in one hospital, shows that the condition is not an extremely rare one and that many cases must be unrecognized.

The condition occurs principally in young girls, or in women during or just after menstruation, or during the puerperium. Five of the 39 cases collected by Hunner and Harris were in children under 7 years. In all cases so far reported, the infection has apparently reached the peritoneum by ascending through the Fallopian tubes. The onset of the symptoms is usually quite acute and the features are those of the other forms of general peritonitis. While these symptoms *may* be of great severity, they frequently are milder than are seen in the other forms of peritonitis, except in the tuberculous form. The collapse is usually not so extreme, and frequently after three or four days of marked symptoms of general peritonitis the condition improves. There are no definite clinical features, however, by which this form of peritonitis may be differentiated from the more severe forms caused by the pyogenic cocci. Symptoms of general peritonitis coming on suddenly in a young child or in a women during the puerperium or just after menstruation, especially if th presence of an infection with gonococci at the same time can be demonstrated by the isolation of these organisms from a urethral, vaginal or cervical discharge, make the diagnosis very probable. This is still more probable if, on pelvic examination, the presence of salpingitis is found. However, recognizing the difficulty of differentiating certain cases of acute salpingitis from those of acute appendicitis, it is questionable whether one is able to make a positive diagnosis in every case.

**Prognosis and Treatment.**—Of the 39 cases collected by Hunner and Harris, 27 recovered, 12 died; and of the 27 recovering, 8 received only palliative and medical treatment. On account of the relative mildness of this form of peritonitis, and the good results obtained by the expectant plan of treatment, the question has arisen as to the value of surgical procedures in these cases. It seems best that, at least until the clinical features are

[1] *Thése de Lyon*, 1901.
[2] Cushing: *Johns Hopkins Hospital Bulletin*, 1899, vol. x, p. 75.
[3] *Johns Hopkins Hospital Bulletin*, 1902, vol. xiii, p. 121.

better known and the means of diagnosis more certain, treatment should be surgical, or at any rate the surgeon should be permitted to take the responsibility of delaying operation.

## METASTATIC OCULAR COMPLICATIONS.

Aside from the primary ocular gonococcus infections, to which reference has already been made, certain other eye lesions may occur, which are manifestly metastatic in origin, and represent either the effect of the gonococcus toxin upon the eye, or are true local manifestations of a general gonococcal infection.

**Metastatic Conjunctivitis.**—There has been much discussion as to whether such a condition really occurs, but from a study of the reported cases it seems probable that a conjunctivitis sometimes occurs during gonorrhœa, in which a direct transplantation of the virus from without can be excluded. In 1866, Fournier drew attention to this form of metastatic conjunctivitis analogous to the metastatic joint lesions. Since then a considerable number of cases have been reported. These have been collected by Carroll, who has also reported a case of his own with a bacteriological report. This form of conjunctivitis must occur with relative infrequency, however, since in the eye clinic of Fuchs, in which 20,000 cases are treated yearly, but 2 examples have been observed. It seems to have certain special features. The symptoms are much milder than those occurring in the ordinary form of conjunctivitis, and the course is much shorter, there being a tendency to spontaneous recovery in six to fourteen days. Both eyes are affected, and the condition is usually accompanied by other metastatic lesions, frequently arthritis and iritis. Recurrences are common. Gonococci have in most cases not been demonstrated either in the secretions or in the conjunctiva itself. On the other hand, they have been found by Lipsly and van Mull. The theory that this form of metastatic lesion may be due to the action of circulating toxins seems to be supported by the experiments of Morax and Elmassian, who produced an inflammation of the conjunctiva by the instillation of the filtered culture medium of the gonococcus into the eyes of rabbits. It was necessary that this instillation be extremely prolonged—from two to seven hours. Nevertheless the conclusions in regard to the pathogenesis of other forms of metastatic lesions apply here as well. The treatment consists in mild antiseptic washes and absolute rest for the eyes.

**Metastatic Iritis.**—This condition is of especial interest, as it usually occurs in association with arthritis, and the clinical features are almost exactly identical with those of rheumatic iritis. This complication occurred 5 times in the 252 cases of arthritis collected by Northrup, and 3 times in Markheim's 52 cases. Among 40 cases of severe arthritis occurring in St. Bartholomew's Hospital, Yeld found 5 complicated by iritis. Of 159 cases of primary iritis, 8 were gonorrhœal in origin. Iritis occurred twice among the writer's 50 cases of arthritis. De Lapersonne gives its frequency, as compared with all other eye diseases, as about 1 in 14,000 cases.

It may occur either as the so-called spongy iritis, or any of the various forms of plastic iritis, and even the hemorrhagic form has been described. Only one eye may be affected, or both may be attacked, simultaneously or in succession. A tendency to recurrence during subsequent attacks of

gonorrhœa has been observed. Practitioners should look on any eye symptom occurring during the course of gonorrhœa with suspicion, otherwise this condition may be overlooked, and when discovered the damage be irreparable.

Mydriatics should be used as soon as possible to prevent adhesions leading to closure of the pupil. Usually the course is mild, and when properly treated, complete recovery is the rule. The treatment is exactly the same as that employed in rheumatic and other forms of iritis.

**Dacryo-adenitis.**—Cases of so-called metastatic gonococcal inflammation of the lachrymal gland have been reported and are collected by Causé.[1] Bacteriological proof of the gonococcal nature of this form of infection has not yet been adduced. In none of the 6 cases collected by Causé did suppuration occur.

Other forms of metastatic eye lesions, either primary, or by extension from one of the above-mentioned forms of metastatic foci, have been recorded, such as tenonitis, keratitis, iridocyclitis, iridochoroiditis, retinitis, neuroretinitis, and optic neuritis. The exact relationship of these lesions to the gonococcal infection is not yet clear.

## GONORRHŒAL SKIN ERUPTIONS.

The occasional occurrence of skin eruptions during the course of gonorrhœa, especially where associated with extra-genital complications, has long been noted. The relationship of these to the gonorrhœal infection has not been clear and even now definite proof of an etiological relationship is wanting. The relatively frequent occurrence of these lesions in severe cases, and the occasional recurrence of the skin lesion with recurrence of gonorrhœa in the same patient, make it altogether probable that specific gonorrhœal skin eruptions do occur. Care must be taken, however, to exclude the cases in which the eruption is associated with certain medication, or, in the more severe cases, with secondary infection. Certain of the hemorrhagic skin eruptions may be due to an associated pyogenic septicæmia, in which such lesions are not rare.

Buschke,[2] who has made a complete study of these lesions, divides them into four groups:

1. **Simple Erythema.**—This is the most frequent form, but in many cases is often but a sequel of certain forms of treatment. It may occur, however, in conjunction with gonococcus septicæmia. In the writer's case of septicæmia mentioned previously, small erythematous patches resembling rose-spots occurred.

2. **Urticaria and Erythema Nodosum.**—Certain of the cases have shown exactly the lesions of erythema nodosum, with raised tender nodes and deep infiltration of the subcutaneous tissue. In most of them there have been joint pains, in some a typical gonorrhœal arthritis. In Buschke's first cases endocarditis occurred also; in the second case pericarditis.

3. **Hemorrhagic and Bullous Eruptions.**—Such lesions have usually appeared in cases with the manifestations of a severe septicæmia, and they are probably (as is quite certainly the case in other infections such as strep-

[1] *Ztschr. f. Augenh.*, Berl., 1904, vol. xi, p. 399.
[2] *Arch. f. Dermat. u. Syph.*, Wien, 1899, vol. xlviii, p. 181.

tococcus) embolic in origin. Paulsen[1] has reported a case of gonorrhœal arthritis in a young child, in which a papulovesicular and bullous eruption occurred over the inner side of the legs and over the face. Smears made from the vesicles, and also from the pus from the joint, showed the presence of gonococci. Cultures, however, were not made and the proof as to the metastatic nature of the skin lesions cannot be considered absolute.

4. **Hyperkeratosis.**—This is by far the most interesting group, as the lesions are apparently specific. These lesions and the clinical features have been more extensively described by Baermann.[2] This lesion is undoubtedly rare, though possibly cases are overlooked. The skin eruption usually follows a severe general infection, usually associated with joint lesions. Owing to this, emaciation and anæmia occur. Then suddenly, on the plantar surface of the feet, palmar surface of the hands, or about the nails, an eruption appears. This may remain localized or become widely distributed over the body. The eruption consists of scaly efflorescences on an entirely re-actionless base. After these fall off, no scar remains. On the hands and feet the eruption may be diffuse and confluent. Often the extremity most involved is the one in which the joint lesions are most marked. With recovery from the joint lesions and other gonorrhœal manifestations, the skin lesion heals of itself. Gonococci have not been found in these local lesions, and the association with the gonorrhœal infection is not clear. The French writers consider the condition a trophoneurosis, due to toxic changes in the nerve endings.

Baermann does not think the crust formation is a true keratosis, but thinks the term *dermatitis papillaris parakeratotica* is better. The condition must be diagnosed from luetic eruption and from psoriasis. Roth also does not consider the condition a true keratosis, but considers that it belongs among the "angiopathic" skin eruptions.

## GONOCOCCUS INFECTIONS IN CHILDREN.

On account of the very great frequency of this condition, as shown by Holt,[3] Baer[4] and others, this subject is of very great importance, not only to the pediatrician and genito-urinary surgeon, but to the general practitioner as well. While of greatest importance in connection with the care of children in hospitals, in which the epidemic occurrence of this infection renders it a most difficult and important problem, it probably occurs in private practice with much greater frequency than recognized or has hitherto been imagined.

The first recorded epidemic of gonorrhœal vaginitis in children occurring in a hospital is probably that of Atkinson,[5] who reported 6 cases occurring in a charitable institution in Baltimore. Baer has collected the statistics from 19 epidemics with 660 cases. The studies of Holt and Reed from institutions for babies in New.York, show that this condition is almost constantly present in practically all of these institutions, and that epidemics of greater or less extent are almost constantly recurring. During eleven years,

[1] *München. med. Wchnschr.*, 1900, vol. xlvii, p. 1209.
[2] *Arch. f. Dermat. u. Syph.*, Wien, 1904, vol. lxix, p. 363.
[3] *New York Medical Journal*, 1905, vol. lxxxi, pp. 521–589.
[4] *Journal of Infectious Diseases*, 1904, vol. i, p. 313.
[5] *American Journal of the Medical Sciences*, 1878, vol. lxxv, p. 444.

in the Babies' Hospital, New York, 273 cases occurred, of which 172 were undoubtedly acquired in the hospital. The disease is almost entirely confined to females, as during this time there was only 1 case of gonococcus urethritis in a male child.

The usual mode of spread in these young children is through the medium of napkins, by the use of baths, or by the use of infected thermometers, syringes, and possibly tongue depressors. The disease is undoubtedly carried from child to child by nurses who care for the infected as well as the uninfected children. The infection may be spread from children with conjunctivitis, as well as those with vulvo-vaginitis or urethritis. The vulvo-vaginal tract of young children must be extremely susceptible to this form of infection, just as the conjunctiva of young children has an increased susceptibility as compared with that of adults. The condition is very chronic and resistant to treatment.

The recurrence of this infection in hospitals can only be prevented by the exclusion of infected children, and this can only be done by the systematic microscopic examination of the vaginal secretion of all patients applying for admission, and by the rigid isolation of all children in whom infection develops, or is only discovered after the child is admitted. Some of the cases are very mild and without bacteriological examination are easily overlooked.

The importance of this infection is dependent not only on the local infection induced, but on the complications which are liable to occur. Endometritis, salpingitis, oöphoritis and peritonitis, frequently leading to sterility, are not very infrequent occurrences. Metastatic foci also occur with considerable frequency. Among them, arthritis is most common, and Holt states that in eleven years in the Babies' Hospital in New York City, 26 cases of gonococcus arthritis occurred, all proven by bacteriological examination. Nineteen of these cases were male babies, and as in only 1 was there other manifestation of gonococcus infection, the mode of joint infection is of great interest on account of its obscurity. Holt expresses a conviction that in these cases the primary infection is through the mouth, though at present there is no bacteriological evidence to substantiate this view. In only 5 cases was but one joint involved, three or more joints being involved in 16 cases, the largest number in any case being eight joints. On account of the difficulty of detecting mild grades of involvement in young children, however, it is probable that multiple joint involvement occurred with greater frequency than the above statistics would indicate. The serious nature of the condition is shown by the fact that 14 children died. In many of these cases, however, there was an associated condition of general marasmus. Many of the cases closely resemble acute rheumatic fever, but this disease is very rare in children under one year. In arthritis in very young children, especially if there occur suppuration, the possibility of its gonococcal nature should be kept in mind. In cases of gonorrhœal ophthalmia metastatic foci, especially arthritis, are not at all rare.

# CHAPTER VI.

## LEPROSY.

By ISADORE DYER, Ph. B., M. D.

**Synonyms.**—Lepra; Elephantiasis Græcorum, Hebræorum; Leontiasis; Satyriasis; Ophiasis; Tzaraath (Hebrew); Kushta (Indian); Juzam Dolfil (Arab); Fa-Fung, Ta-ma-Fung (Chinese); Boasi (South American); Lebbra (Italian); Radesyge, Spekalshed (Norwegian); Aussatz (German).

**Definition.**—Leprosy is an endemic disease, contagious in type, due to the direct presence of the *Bacillus lepræ*, which in its development produces structural changes in the skin and mucous membranes, nerves, bone and other tissues, usually resulting in more or less alteration in the configuration of the tissues involved, at times causing actual deformity and mutilation.

**Historical.**—The early history of leprosy is obscure, even confusing. The Bible references[1] to the disease are sufficient to establish its existence, but the descriptions are inaccurate and the leprosy of ecclesiastical literature seems to have been generic for a number of skin affections. Both the Talmud and the Koran take cognizance of the disease and apocryphal writings discuss it. Knowledge of early leprosy appears to have restricted the disease to Egypt and the Orient and in India the disease was recognized as early as 1500 B.C. In 600 B. C. the Persians instituted measures against leprosy (Leloir).[2] As early as 636 A. D. lazarettos were established in Italy. In the tenth century the islands of Great Britain were afflicted. In the eleventh and twelfth centuries the disease spread all over Europe, directly attributed to the returning crusaders. Measures were adopted for its control, chiefly consisting in the establishment of leprosariums. Of these it is stated there were 19,000 in Europe, and 2,000 in France alone. The colonies of European countries suffered next, until to-day there are few lands free of the disease and it is estimated that there are nearly 3,000,000 lepers in the world. Of these, the largest number is in China (estimated at 2,000,000); the next is in India (estimated at 200,000); while the other parts of the world afflicted are the following: Japan (20,000 known lepers);[3] Northern, Eastern and Southern Africa; Madagascar; Arabia; Persia; Russia; Norway; Sweden; Italy; Greece; Spain; (Germany, France and Austria, excepting Hungary, are practically free of the disease); the islands of the Pacific and Indian Oceans. Leprosy is also endemic in Central and South America. The United States of Columbia, Ecuador, Venezuela, Brazil, Chili and Peru have each recorded statistics concerning the disease. In Mexico and in almost all of the islands of the West Indies leprosy is found and in most of these provision is made for it.

In North America a number of the United States are involved, notably Louisiana, California, New York and Minnesota. In Louisiana the disease

[1] *Exodus* IV, 6; *Leviticus* XIII, 24, 25, 43, 52; *Numbers* I, XIII; *Deuteronomy* XII.
[2] Leloir: *Traité de la Lèpre*, Paris, 1885.
[3] *Transactions of the Berlin Lepra Conference*, 1897.

is endemic, occurring almost wholly among the native born or persons long resident in the state, while other centres show simply an increasing number of cases in recent years. Since 1905 about 400 cases have been recorded in the United States.[1] New Brunswick in Canada, at Tracadie, and British Columbia, at Darcy Island, have a few cases.

The numerical importance of the disease has carried considerable force with various governments to the end that legislative action, aimed at segregation, control and treatment, has become general. In some countries the provisions are fulfilled under private charity but for the most part government provision of funds has accompanied the execution of enactments. These results have followed the Berlin Lepra Conference of 1897 and in all countries an intelligent effort is now being made to accomplish a better knowledge of leprosy and its eradication, through sanitation and treatment.

**Etiology.—Contagion.**—The consensus of opinion has accepted the *Bacillus leprœ* as the cause of leprous lesions and their effects and the evidence points to the introduction of the organisms of the disease through the nasopharynx. This theory is strengthened by the absence of an initial lesion of leprosy at any particular point of inoculation, the absence of specific inoculation or the history of such, and the frequent occurrence of the disease under conditions which favor the inhalation of the disease-bearing secretions from the original case. Frequent cases in the same family, the spreading of the disease in districts and in cities, countries, and states, suggest the more likely spread through the respiratory tract.

Among those who have strongly urged this theory are Goldschmidt, Morrow, Sticker, Jeanselme, and others (Babes, Gluck, von Peterson) more recently. Emilio Martinez, of Havana, personally stated to the writer that in almost every patient with leprosy he had been able to examine, he had found an early excoriated lesion in the nasal mucous membrane showing the bacilli of the disease.

**Heredity.**—Heredity is still held a factor by a few observers but the vast majority have dismissed it as a consideration. The results of the British Leprosy Commission in India in 1893 showed less than 3 per cent. of cases developing among children of lepers removed at birth and these showing the disease after the third year; the absence of any record of a leper born as such in any of the many centres of the disease still places the burden of proof on the few who claim this as a factor.

**Race.**—Race undoubtedly bears a close relation to the spread and to the element of susceptibility to the disease. Records in almost every country show the native born the most frequent victim while the foreigner is slow to acquire the disease. This is particularly exemplified in China, Japan, India, the Hawaiian Islands, the Philippines, Colombia, the Polynesian Islands, Madagascar, Mexico and Louisiana. There is no doubt, however, that the likelihood of exposure to contagion is more apt to occur in the family and community life among these, and this must, therefore, be taken into consideration.

**Diet.**—Quite a number of leprologists have urged diet as an element in the spread of leprosy and the prominence of some of these protagonists demands a consideration of the theory. Jonathan Hutchinson has supported the fish origin of leprosy for many years. His observations and deductions

[1] "Leprosy in North America" (Dyer), *Transactions International Dermatological Congress*, Berlin, 1904. The author's notes record 219 cases in Louisiana.

have been almost entirely derived from British India and as yet the theory is unproven. Ashmead, Blanc and others have expressed a belief that fish may be the occasion of leprosy. Hutchinson propounds the idea that leprosy occurs chiefly in India among fish-eating peoples who are not particularly careful about the freshness of the food; others argue the possibility of fish acting as the intermediate host for the leprosy bacillus. As yet no one has discovered the bacillus of leprosy in fish or in any other food supply and the disease occurs alike in those who eat fish and those who have no fish to eat. Almost as a unit the students of leprosy in India, the Hawaiian Islands and in other leper centres deny the evidence of any such origin. The observers in India point rather certainly to widespread occurrence of the disease among those castes who by religious obligations are forbidden fish.

Diet in its relation to the individual leper is another matter and particular emphasis is laid upon its importance as it may affect the resistance or otherwise to the disease.

The habit of oral feeding of infants in the Hawaiian Islands and the family promiscuity in eating "poi" with the fingers is held as possibly accountable for the spread of the disease by contagion.

**Climate.**—Warm climates evidently favor the development of leprosy but it occurs in any climate as is exemplified by the long prevalence in Norway, Sweden, Iceland and Japan. Seaboard countries seem to have suffered most from the disease but this is easily accounted for as these are naturally most exposed through their ready intercourse with infected countries through ordinary ways of commerce. Leprosy spreads, however, in every country where it is introduced. Where community life, hygienic environment and standard of metabolism are high, the disease does not spread rapidly.

**Vaccination.**—Vaccination has been discussed as a probable method of the spread of leprosy but no proof has followed the tentative theory and in these days of bovine virus such a likelihood is precluded.

**Insects.**—Recently the proposition has been made that fleas might be the medium of spreading leprosy. Mosquitoes, bedbugs, and other accidental parasites attacking the human body have been considered in the same way. Nuttall reviews the various opinions on this point, and considerable work was carried on by the British Leprosy Commission without result. Within the past six months, E. S. Goodhue, of Holuloa, Hawaiian Islands, has announced the finding of the *Bacillus leprœ* in mosquitoes and in bedbugs.

**Other Diseases.**—Fitch of San Francisco and some adherents argued the possibility of leprosy as a "fourth stage" of syphilis, but so many cases of syphilis contracted by persons already lepers have been reported that the theory has fallen, even if other evidence had not sufficed. The identity and correlation of leprosy and tuberculosis is a more recent idea which has been rather ventured than tried.

While the contagiousness is capable of only indirect proof the vast amount of evidence points to this as the sole method of spread of the disease, and as more exact opportunity is now afforded to study early cases, it is likely that an initial lesion may be found, particularly as that has already been suggested as probably present in the nasopharynx.

**Pathology.**—Every evidence of leprosy in the human economy is essentially due to the lepra bacillus, no matter what organ may be affected. This has been firmly established since the original discovery of the bacillus by

Hansen in 1868. The *Bacillus leprœ* is described as a small rod bacillus, from one-half to three-quarters of the diameter of a red blood corpuscle in length ($\frac{1}{5000}$ of an inch) and in breadth about one-fifth the length. According to Cornil, the largest are found in the parenchymatous organs, while in the skin lesions they are less developed owing to compression. The bacillus is straight or slightly curved, with pointed or rounded extremities. It occurs in short chains or beads, resembling the tubercle bacillus, and may have its extremities club-shaped (Byron). The lepra bacilli are more abundant than the tubercle bacilli and are more frequently found in clumps and masses in the tissues and are more readily stained with the usual methods. In instances of doubtful determination, inoculation experiments establish the diagnosis of tuberculosis and exclude leprosy. Arning's inoculation experiment with a Hawaiian leper (Keanu), in 1884, has been discredited owing to the strong probability of contagion from near relatives who were lepers.

In animals, Damsch, Campana and Vossius succeeded in reproducing the disease *in loco*, but not generally. Melchior and Ottmann succeeded in distributing the disease to the visceral organs, etc., following the introduction of a freshly extirpated leprous tubercle into the anterior chamber of a rabbit's eye. Experiments with the human subject have been rare and without authoritative verification (Daniellson and Boeck). The bacillus may be found in almost any tissue, but is selective of particular organs, tissues and regions. The bacillus occurs in the nasopharyngeal and other secretions, the saliva, the fæces, vaginal and urethral secretions, and in the semen, milk and sweat. Sticker claims that the presence of the bacilli in such large numbers in the nasal secretion commends the early examination of this as a means to diagnosis. The fluid from artificial blisters as well as serum drawn from deep tissues have been examined for the bacilli with positive results.

The smears from these secretions and fluids are dried and fixed in the ordinary way and stained with carbol-fuchsin, as for tubercle bacilli, decolorized with a weak solution of acid (3 to 5 per cent.), completed with alcohol and counter-stained with methylene blue. The cigar-bundle shaped masses take up aniline stains (Gram method) at the room temperature and retain them tenaciously. Unna recommends staining in a twenty-four hour old Ehrlich's solution newly filtered for twelve to twenty-four hours at the room temperature or one to two hours in the incubator, wash for ten minutes in water, and place in 20 per cent. nitric acid until greenish-black. Wash in absolute alcohol until pale blue and in water until colorless; dry and mount.

Attempts[1] at culture of the bacillus have met with varying results. Byron made a pure culture in agar-agar. Bordoni-Uffraduzzi, Babes, Czaplewski, Spronk and Kedrowski claim to have succeeded. The organism grows slowly and the cultures resemble those of the tubercle bacillus. The organisms, however, differ from those found in the body in not being acid-fast and it is questionable if they are identical. The media used were mixtures of blood serum, peptone and glycerine. The glycerine seems to be essential.

The bacilli are widely disseminated throughout the body, having been found in practically every organ and including the peripheral nerves, spinal cord, brain, and in the skin (even in scrapings of the skin), interstitial con-

[1] Babes: "Die Lepra," Nothnagel's *Pathologie und Therapie*, XXIV Bd., 1901, Wein. (A very complete bibliography on leprosy is given.)

nective tissue and in the muscles. In general the number of bacilli has no relation to the severity of the accompanying tissue changes.

Scheube[1] gives a comprehensive summary of tissues where the bacilli have been observed:

The skin and mucous membranes, earliest in the anæsthetic patches.

In the peripheral nerves and lymph glands, especially in the sheaths and in the lymph gland secretions.

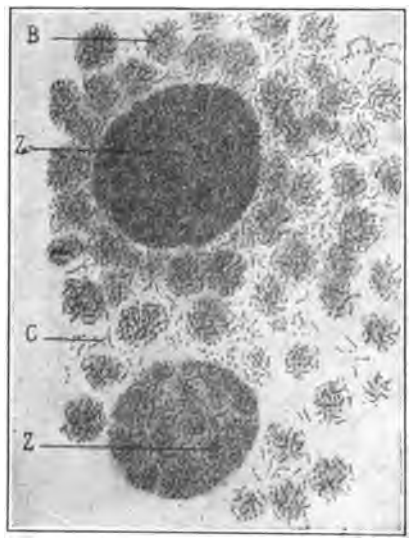
The internal organs involved are the lungs, liver (especially the liver cells), the intestines, kidneys and lumen of the urinary tubules, the testicle, its tubules and ducts, and the ovary.

In the tonsils, the eye, in the sweat glands, hair follicles and sebaceous glands between the epidermal cells, and in the arrectores pilorum the bacilli are found.

The connective tissue of the cutaneous nerves, in the Pacinian corpuscles, the salivary glands, pancreas, adrenals, spleen, larynx contain the organisms. They are also found in the substance of the brain and cord and in the Purkinje cells of the cerebellum; in the choroid, retina and ciliary body; in the muscles and tendons, and in the periosteum, bone and medulla. In the acute stages of leprosy, the bacilli are found as contents of the blood cells and in fluid lesions of the disease. The bacilli are very numerous in the infiltrative tissues, and in nodules and tubercles, but in the erythematous patches and nerves they are scanty.

Outside the human body the bacilli have been found in the habitations of lepers and in the ground over lepers' graves. Various fish have been examined for the bacilli but with negative results.

FIG. 4.




*B*, bacilli in groups; *ZZ*, zooglia masses—giant cells; *C*, chains of bacilli. (Leloir.)

The leprous nodules belong to the group of granulation tumors and are similar to those of syphilis and tuberculosis. Microscopically they consist of a small amount of fibrillar connective tissue with numerous cells of various forms, mostly small, round epithelial cells, spindle formed, and the leprosy cells. These are mostly large, round or oval cells, with many nuclei and vacuoles. They contain the leprosy bacilli. These cells are diagnostic of the disease and are found most numerously in the tubercles and nodules of leprosy. Neisser observed the gradation in the development of the lepra cell in size and contained nuclei and bacilli, also the degenerative lesion showing numerous extra-cell bacilli. Virchow, Neisser, Gerlatz, and others argue the consistent type of the lepra cell as the container of the bacilli, the exception being

[1] *Die Krankheiten der Warmen Länder*, IIIer aufl., Jena, 1903, pp. 320–392. (With a very complete bibliography.)

against the rule; Unna is the chief protagonist of the "extra" cell theory, claiming that the lepra cell is only a mass of agglutinated bacilli, which are habitually aggregated in the lymph spaces.

In the trophic, or nerve type, the changes are found in the peripheral nerve trunks and their cutaneous branches, the central changes occurring secondary to general changes or infection. The leprous deposits are especially found in nodules along the ulnar, median, radial, musculo-cutaneous, intercostal, humeral and peroneal nerves. Thickening of the nerve is common. The trophic changes follow the invasion of the nerve itself by the bacilli.

**Symptoms.**—The uncertainty of fixing any particular period of incubation and the lack of observation of the early stages of the disease compel a study of the preliminary symptoms only upon the subjective history and after tangible manifestations are in evidence. Even in leprosy centres, suspicion of the disease arises only when local conditions appear and premonitory signs of the disease have been ignored. That these do exist many observers agree and the arrangement of these is based upon a supposed period of incubation, as this cannot be exactly known. The history of exposure is usually absent and, even when ascertainable, the length of time is too variable to admit of any accurate statement. This period varies from a few weeks to many years. Some instances are related in which twenty years had elapsed since known exposure to the disease had occurred. Continuous exposure over long periods has been noted, however, in the instance of several members of the same family or community being affected and here the prodromal symptoms have been studied.

The one most constant symptom is the occurrence of fever, intermittent and irregular in period and in type. Malaise, anorexia, dyspepsia, epistaxis, dryness of the nasal and respiratory passages, vertigo, headaches, neuralgias, pains in the arms and legs, and exaggerated functions of the fat and sweat glands are among the notable symptoms. The sweating is particularly striking, as it is periodical and evidently associated with nervous disturbances. There is in all instances a sense of anxiety, of anticipated calamity.

There may be marked hyperæsthesia of the skin, shown in areas of pruritic exaggeration with localized neuralgias. The intestinal tract may be disturbed by frequent diarrhœa and as a result it is quite usual for the patient to lose in weight.

So far as the specific manifestations are concerned, the usual diagrammatic method of resolving leprosy into fixed types is faulty and often misleading. While these certainly come under observation, the unusual cases are the rule. The evidences of leprosy are directly due to the invasion of the *Bacillus leprœ* and according as any particular organ or tissue is involved the symptoms are manifest. While any organ or tissue may be attacked, the vast majority of patients show the skin and the nerves as the selected sites.

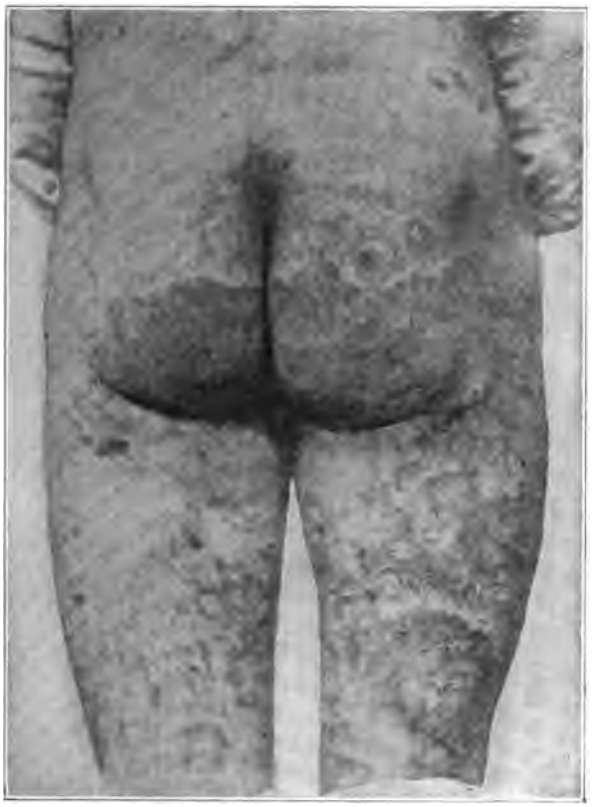
Dependent directly upon the degree of this invasion and upon the individual resistance, are the evidences in the skin and in the nerves themselves. In the history of every patient some logical course is followed in the expression of the disease but all do not follow exactly the same development. If the skin shows the first evidence, this may appear either in explosive lesions, as bullæ, in simple erythematous patches, or in exactly localized areas of bacilli colonized in masses and forming tubercles.

When the nerves are attacked, along the course of the nerve involved there is either thickening of the sheath or of the nerve itself, or nodes of varying

size are formed. At the terminal ends of the branches of these nerves, skin lesions in the form of bullæ, pigmentation, thickening or atrophy of the epidermis may appear or there may be actual neuritic changes in the muscles, tendons and bones.

Skin leprosy presents its several lesions either separately or together at the same time and while the macule often occurs as a preliminary eruption it may be the sole evidence of the disease. So with the tubercles of leprosy. These may appear at once or may develop upon the areas previously outlined by the erythematous or macular eruptions. All of these lesions may occur

FIG. 5.



Macules of leprosy. (Leloir.)

together and again they separately or together are often found concomitant with the nerve lesions and changes, which they may also precede or follow.

The first evidences of skin or nerve leprosy are the bullæ, found upon the extremities, especially on the hands and feet. With skin leprosy these are usually small in size, numerous and superficial. They occur bilaterally and symmetrically, usually on the dorsum of the hands and feet and especially over the fingers. They break quickly and dry, leaving a superficial erosion which heals spontaneously, and the site of the lesion is marked by a white scar, usually with a pigmented and irregular border.

With nerve leprosy these lesions are more often single, large, and occur over the joints of the phalanges; as a rule they persist, even ulcerating deeply at the point of origin. Even if healing should occur, there is a tendency for a new lesion to form at the site of the scar and ulceration develops, causing necrosis of the area affected. As any joint of any finger or of all fingers may be involved, the process may be progressively destructive, resulting in actual loss of one or more of the phalanges, either distal or intermediate. The process may start at the end of the digit, involve the nails, and result in the ultimate destruction of the whole digit, leaving the hand or the foot minus fingers or toes respectively.

The erythematous eruptions are evanescent or permanent. In the first instance they occur as the evidence of a general infection and come as an exanthem. They select particular regions, notably the cheeks, shoulders, buttocks, thighs and legs, sometimes the arms, forearms and hands. The eruption is bilateral, symmetrical and marked by an irregularity in the size of the areas involved, which are sometimes no larger than the thumb nail, while again the area may involve the whole of the region affected, as over the buttocks. The patches are deep red in color, do not fade entirely on pressure and have a suggestion of turgescence in a certain amount of elevation and rounding of the lesions. In a few days or weeks these disappear and may not recur. Oftenest, however, the areas over the buttocks, thighs, legs and shoulders remain defined as they first appear, growing dusky red in color, often mottled and thickening with age. The periphery grows more elevated and thickened, also increasing in depth of color to a brownish-red, while the centre fades to a buff or even to a dirty white. The patches grow somewhat elliptical in shape and remain in this general form and with this consistency throughout, or the borders break up into distinct masses of tubercles, each representing a colonized accumulation of the bacilli. When the face is involved there is often confluence of the erythematous areas making a mask over the whole of the face, and involving the neck and ears. Here the thickening destroys the normal expression and produces a fixed, satyr-like appearance giving rise to the term "*satyriasis*," sometimes applied to the disease. The nose, ears, lips and eyelids become pendulous, occasioning a marked interference with the circulation and a consequent swelling. Ectropion follows and a bleary stare results. With the general thickening, the face rolls in folds and forms in parallel masses covered with a shining telangiectatic, smooth or tuberous, sometimes fis-

FIG. 6.

Satyriasis. Tubercular leprosy. (Cooper.)

sured, skin; the lips grow swollen and everted and "*leontiasis*" has developed.

Nerve leprosy seldom extends beyond the developments of the disease at the extremities. Here and there along the ulnar and sciatic nerves and their branches, on the surface of the skin an erythematous eruption may appear, usually only temporary and expressing some fresh leproma of the nerve. Of course the processes in nerve leprosy may go on at the same time that skin leprosy develops and it is usual to see the one or other superimposed as the condition progresses. One rare instance of a correlation of nerve and skin leprosy is the atrophic type. Here, consequent upon the erythematous eruption and the pigmented areas, a general atrophy of the skin occurs, the muscular and keratin elements in large degree disappearing and leaving a true skin atrophy, with loss of the appendages, including the whole of the hair, the nails, and loss of function in the glands. Emaciation follows rapidly and death is swift.

FIG. 7.

Leontiasis. Terminal Stage of Tubercular Leprosy. (Cooper.)

Tubercle leprosy is essentially skin leprosy. The location of these lesions is not constant but they have sites of predilection. The face presents these on the forehead, nose, alæ nasi, lips, chin, cheeks and ears. The arch of the eyebrows is a frequent site. The hands and feet, legs, thighs, buttocks, shoulders and forearms are the next in order of frequency.

The leprosy tubercle may be single, clustered, disseminate or diffuse.

The single tubercle is usually large, more or less flat and found on the face, cheeks, hand or forearm; usually few occur. The color is bright brownish-red with the centre of the flattened lesion lighter than the border. The clustered tubercle is usually rounded, closely aggregated and selective of the alæ nasi, ears, chin, hands and lower third of the leg; the buttocks may also be involved. These lesions occur with a classical bilateral symmetry and are characterized by the almost olive and red color of the skin involved.

The *disseminate* leprosy tubercle is small, about the size of a pea, hard and round, uniform in size, occurring generally over the body, bilaterally and symmetrically; the lesions are separated by areas of clear skin and distinguished from all other tubercles by the waxy white appearance, as if white wax showed through a dirty brown transparent covering. Almost always this type of skin leprosy argues the occurrence of like lesions in the thoracic and abdominal viscera, as these cases rapidly become acute and result fatally in short order.

In each of the varieties of skin and nerve leprosy, and especially in the former, there are periods of quiescence and exacerbation. A striking feature in the periods of exacerbation is the "lepra fever" mentioned by a number of

observers. C. B. Cooper, Chairman of the Committee on Leprosy of the Hawaiian Government, has best described this phase of leprosy, although the condition seems more severe in his locality than elsewhere. He calls the condition "swollen head fever" as this was the term given it at the Hawaiian settlement at Molokai. He describes this as "an acute, epidemic, painful, inflammatory leprous fever, in which the head and face become greatly swollen, and in which the lymphatic and glandular system becomes characteristically involved, especially the cervical and sometimes the axillary and inguinal glands as well." He was able to find the leprosy bacilli in the blood during the stage of fever. Concomitant with this condition is a typical lepra exanthem, differing from any of the eruptions above described. Cooper lays no stress on this, but, in the writer's observations at the Louisiana Leper Home, these were frequent enough to be considered important. The eruption consists in the occurrence, almost universally over the body, of bright red papules, lentil shaped and uniform in size, usually hyperæsthetic and at times painful, even severely so. With lessening of the general symptom, the eruption disappears, usually leaving, however, an increase in number in the previous lesions.

FIG. 8.

Single lesions. Tubercular Leprosy. (Cooper.)

**Altered Sensation.**—So much stress is laid upon this that special attention should be given to it. All skin lesions in leprosy excepting the evanescent erythema and the exanthem of papules in leprous fever are anæsthetic to pain, sometimes to touch, heat and cold.

Hyperæsthesia is marked in the prodromal period and sensation is exaggerated in the exanthematous lesions. With nerve leprosy, hyperæsthesia is marked for weeks and months before the evidence of an affected nerve is complete. This is shown in pain along the extremity and in the hands and feet. Often distinct points of pain are recognized. As soon as the nerve is thickened and the nodes are formed, anæsthesia becomes complete along the areas of cutaneous distribution of the nerve involved. Usually the anæsthesia begins at the distal end of the nerve and travels toward the source. The little finger is usually the first point of anæsthesia noticed, and more often on the left side.

**Effete Leprosy.**—The leprosy in Brittany and that in the Orient, as well as many cases found in old leprosy centres, presents types which seem to show no acute symptoms at all, but which evidence trophic changes of slow development and unattended with inflammatory processes. Zambaco-Pacha and von Duhring have described these and most of them are of pure trophoneurotic type. They present the claw-hand, loss of phalanges, facial paralysis, etc., usually considered as sequelæ of nerve leprosy.

**Sequelæ.**—As the direct result of leprous changes in the body, destructive processes in the internal organs, ultimately producing death, may result. Hillis tabulates the causes of death as marasmus (38 per cent.), septicæmia

FIG. 9.

Nodular leprosy. (Cooper.)

or intercurrent disease, as nephritis, (22.5 per cent.), pulmonary diseases, including tuberculosis, (17 per cent.), diarrhœa (10 per cent.), anæmia (5 per cent.), remittent fever (5 per cent.), and peritonitis (2.5 per cent.).

The natural necrosis, attending the final degeneration of tubercles, results in the loss of the nasal bones, often of the nose itself; in the ulceration on the face and in involved areas there is scarring, with contracting cicatrices, producing facial and other deformity. Most trophic nerve types develop one or more ulcers at the extremities, with consequent destruction of tissue. According to the limit of the process there may be simple contraction of muscles, atrophy of bones and subsequent deformity, or the whole of the member involved may slough off.

**Diagnosis.**—The customary observer of leprosy needs little aid to a diagnosis, as the facies, the color, and the classic lesions are well known to him. So much responsibility, however, rests in determining leprosy that due care should be exercised by those to whom it is a casual disease.

The diagnosis is absolute when destructive lesions exist in which the lepra bacillus may be demonstrated in section, in the fluid contents, or in culture. Clinically there should be little difficulty if the cardinal features of the disease are kept in mind. The essential points may be summarized as follows:

1. The habitat, community or domicile, suggesting exposure.
2. A history of exposure or contact with persons affected.
3. Eruptions or bullæ on the extremities.
4. Areas of discoloration with anæsthesia.
5. Trophic disturbances: (*a*) Perforating ulcers; (*b*) muscle atrophy, especially of the hands, determining the "claw-hand"; (*c*) clubbed fingers; (*d*) deformity of the hands and feet from loss of phalanges; (*e*) persistent ulcers at the articulations of the phalanges of the fingers and toes; (*f*) facial paralysis.
6. Discolored and blunted nails.
7. Symmetrical eruption of macular areas with bilateral distribution: (*a*) Marked by dusky red or "café-au-lait" discoloration; (*b*) with elliptical shape, the peripheral ring being elevated and deeply pigmented, while the

FIG. 10.

Trophic leprosy. (Leloir.)

centre remains lighter or a dirty white in color; (*c*) marked anæsthesia throughout these macular areas; (*d*) a predilection for particular regions, notably the buttocks, legs and forearms.
8. Tubercles with typical modes of appearing and of distribution.
9. Loss of expression in the face; satyriasis, leontiasis; ectropion of eyelids and of lips; furtive look in the eyes.
10. The early involvement of the nasopharynx and the larynx, resulting in a characteristic involvement of the vocal cords, determining a peculiar metallic resonance in the speech which is distinctive. The note is nasal and raucous.

Particular diseases mistaken for leprosy are few and the differentiation easy:

*Erythema multiforme* presents lesions which are evanescent, fade on pressure without pigmentation and are not anæsthetic.

*Syphilis* is differentiated by the color of the lesions, the symmetrical distribution of the leprous tubercles, their anæsthesia and course of development.

*Sarcoma* (multiple) by the pain, the size and course of development, the color and consistency.

*Lupus vulgaris* by the color, distribution, consistency and method of development of the lesions. The examination of the section or culture is sometimes necessary.

*Morphœa* by the absence of anæsthesia, and the color.

*Raynaud's disease* by the progressive ulcerative process, limited to the extremity involved, and by the absence of the nerve trunk involvement. The leprous perforating ulcer is nauseating; the ulcerating lesions of Raynaud's disease are simply offensive in odor.

FIG. 11.

Claw hand (Griffe) of nerve leprosy. (Leloir.)

*Syringomyelia.*—So many observers have related cases of leprosy possessing all the features of this disease and it so often occurs that cases diagnosed as syringomyelia are subsequently proven leprous that it is impossible to differentiate these except through finding the lepra bacillus, or postmortem evidence of changes in the cord without leprous involvement.

**Prognosis.**—Leprosy is like all other bacillary and infectious diseases; it is self-limited. Its evidences may last for years, or only for weeks or months. Often the disease will have periods of abeyance and exacerbation. Most often the course is run to a fatal issue or the victim may present scars or mutilation as the final expression of the spent morbid process. The

average duration is about eight years. The mixed and tubercular are the more rapidly concluded, in from four to twelve years, unless shortened by some intercurrent disease. The spontaneous involution of lesions may be followed by no recurrences, but this is usually only a process in the final result, though the longevity of the individual may be increased by this remission.

**Treatment.**—Until recent years the sole treatment was directed to sanitary control, in some countries administered under barbaric restrictions and methods. To-day most countries afflicted with the disease are provided with hospitals and asylums, the majority of these being under hygienic regulations so far as habit and food are concerned. Only a few leper institutions maintain systematic medical supervision of the disease itself, but the inclination is to expand the measures of amelioration for the inmates. In some asylums where leprosy has been studied and treated, a direct result has been obtained in a reasonable time. In some instances leprosy has been reported cured. This is true of the work of Rost in India, Goldschmidt in Trinidad, Tonkin in Jamaica, Carrasquila in Colombia, and of the work in Louisiana. Besides this, individual cases are occasionally reported as cured. The most striking thing in the reported cures is the variety of remedial measures employed. From the radical sanitary and individual measures employed in the time of Moses down to the latest serum devised by Rost, the number of leprosy remedies has grown vastly. We cannot as yet proclaim a specific but we may draw deductions as to the therapeutic indications.

In all cases under treatment the progress in amelioration is slow. On the other hand, the disease may be absolutely self-limited without treatment, the evidences disappearing without a relapse or recurrence. The result of treatment depends directly upon the individual patient and upon the resistance he possesses or may acquire against the morbid process.

The treatments which have availed most have been supportive and hygienic. Drastic or reducing methods aimed at specific action have been temporarily remedial, but the disease re-awakens usually in the depleted subject. Serum treatment has been attempted, but hitherto has been successful almost solely in the hands of the one introducing it. Rost's serum is too new to have a final judgment.

The treatment of leprosy may be arranged in several divisions according to the method employed, *viz.:* alterative; supportive; empirical; serum; sanitary; and surgical.

The alterative treatment has been based upon the idea that such medication would reduce hyperplastic conditions and aid their absorption. Remedies so employed have been bichloride of mercury (Crocker), salicylate of soda and salol (Hawaiian Islands), europhen (Goldschmidt), chlorate of potash (Chisolm, Carreau) and the iodine salts. The results have been variable, though Crocker has reported 2 cases and Hutchinson 1 case evidently cured by hypodermic injections of the bichloride of mercury; Goldschmidt used europhen hypodermically successfully and Gruenfeld of Odessa confirmed this result; all of these cases have been isolated instances, however, arguing the first conclusion that the resistance is the essential factor.

Supportive or tonic treatment includes such remedies as hoangnan, strychnine, arsenic (Hutchinson and G. H. Fox), mercurial salts, general tonics, each of these having a particular champion for the time being.

Empirical treatment has had a continuous history, even to the present when every now and then some new discovery is brought out. That much

good has been accumulated by experimental use of remedies is true, but no exact deductions have been drawn in the study of those measures.

India has supplied most of the drugs employed. Chaulmoogra oil seems to have survived almost all the other herbaceous remedies and is now extensively employed universally. While this may stand as an empirical remedy it must also be considered as supportive, as the oil is in large part assimilated. The dosage depends upon the patient, but to be effective this should be increased to 100 to 150 drops at the dose, or 300 to 450 drops a day. Beginning with 3 to 5 drops of the oil in capsule, coffee, hot milk, or cordial, the dose may be increased gradually to tolerance. The oil may be given in pill form, combined with tonics, as iron, arsenic and strychnine or nux vomica. The consensus of opinion places chaulmoogra oil first among all remedies hitherto suggested. More cures have resulted from its use than from any other one remedy, and within a few weeks after its use amelioration is noted, even in advanced cases.

South America has contributed two remedies, assacon (*Hura braziliensis Martin*) and tua-tua, both used in the green state by macerating the leaves or berries and giving the resulting liquid. The reports on these are meagre and questionable. The red mangrove, or mangle, has been used in Key West and Havana. First suggested by a Key West druggist, this remedy was extensively exploited by M. Duqué of Havana. The powdered bark and root, used in tincture or pill, and also employed in the bath, were experimented with. Only one patient was relieved of symptoms by this treatment and doubt was thrown on this because of previous treatment with chaulmoogra oil.

Ichthyol and the mixed toxins of erysipelas, tuberculosis and vaccinia, are among other empirical remedies without marked result. Unna reported improvement under ichthyol but he abandoned this for chaulmoogra oil.

The Fiji Islands practice a scorching process which has its merits: the patient is placed upon a pyre of green leaves of a tree supposed to be specific against leprosy. In the slow process of cooking which the skin receives, the disease is supposed to disappear, and if the victim survives, he is expected to recover.

The West Indies and some parts of South America carry the superstition that the bite of a venomous reptile will cure leprosy and occasionally a native victimizes himself to this end. Influenced by the report of the condition resulting from the accidental biting of a leper by a viper in the West Indies the writer used the antivenomous serum of Calmette in a series of patients, with almost uniform good results. Three of the patients recovered. Injections were made at frequent intervals, sometimes daily, and the dosage varied from 5 to 20 cc. The buttocks and the shoulders were the usual sites of injection, though frequent injections were made in the lesions themselves, with the interesting result that these were directly influenced to favorable resolution. The cost of the treatment precluded extensive experimentation, so normal horse serum was employed in the same manner in a new series of cases but without result.

The sera of Carrasquilla and of Laverde, derived from the leprosy bacillus and tissues, may be mentioned. Both were successful to a greater or less degree at the hands of the originators, but failed elsewhere. Quite recently a new serum has been introduced by Rost of the Indian Medical Service. This, which he calls "leprolin," is derived from a toxin of the *Bacillus leprœ*.

Cultures of the lepra bacilli in special media were allowed to grow for six weeks at a temperature of 37° C., then sterilized and passed through a Pasteur filter, when glycerine was added. The dose of leprolin is 10 cc., equivalent to 50 cc. of pure culture of the bacillus. The injection should be made into the muscles of the buttocks or of the arm. Two or three days is the usual interval, but both the dosage and the interval are regulated by the reaction and the dosage is increased if a reaction of 100° F. does not occur. By increasing the dose in this way a proportionate improvement has been observed. Leprolin is contra-indicated where pulmonary or kidney complications are present. In conjunction with the treatment, salt is freely administered and equal parts of salt and vaseline are rubbed into the anæsthetic areas.

In every patient under treatment, marked improvement was noted and of 120 cases treated, 14 were discharged as cured, and a number of others are rapidly recovering sensation with loss of leprous evidences. Unfortunately no confirmatory experimentation has been possible, owing to the limited supply of serum, but the published results are most encouraging.

Treatment resolves itself into the essential fact that the disease is one in which a method of reconstruction is necessary, based upon hygiene, diet, and medication. Experimental treatment should be secondary to well-known practice and only where evidence of improvement under recognized treatment is absent. Treatment above all must be constant and the patience of both physician and the patient must be great.

The regular practice with the writer is to insist upon daily hot alkaline baths, a liberal diet without indigestible food, and a regular dosage with strychnine in $\frac{1}{60}$ to $\frac{1}{30}$ gr. doses (1 to 2 milligrams). Arsenic, iron, the phosphates, olive oil, etc., are given selectively. The majority of patients are treated with chaulmoogra oil, but now and then some other treatment is indicated. Under this general regime, 12 cases of leprosy have been cured since 1894, (10 of these have already been reported[1]).

Surgical treatment is directed at the condition present and consists in amputations, nerve stretching and electrotherapy. The use of *x*-ray treatment may be mentioned. Gilchrist succeeded in reducing the tubercles after a number of exposures. Similar reports have emanated from the Philippines but as yet radiotherapy must be entertained only as an aid.

So far as concerns the United States in the general sanitary care of leprosy, Congress has enacted several bills, directed at the investigation of the disease, and in February, 1905, a bill was entertained looking to a national leprosarium. As yet nothing has come of this. Meantime, Louisiana regularly cares for her lepers in a model home under hygienic and systematic medical administration. The rest of the United States takes little interest in the subject, excepting San Francisco, where a large Chinese contingent compels a system of segregation. Massachusetts has established a temporary asylum for five lepers on an island in Boston Harbor.

Earnest effort throughout the world promises relief from the disease in one or another way—either by obliterating it by segregation or of finding a panacea.

[1] *Medical News*, New York, July 29, 1905.

# CHAPTER VII.

## TUBERCULOSIS: HISTORY AND ETIOLOGY.

By EDWARD R. BALDWIN, M.D.

### HISTORY.[1]

**In Antiquity.**—Pulmonary tuberculosis, consumption, or phthisis has existed from very remote times. It transcends all other maladies in the total number of its victims and the cost to society in civilized countries. Tuberculosis was a disease familiar to the most ancient civilizations, judging from the cuneiform inscriptions on tablets found in Babylonian remains, which represent the earliest known human records. Whether or not it existed in the most primitive state of man is a question without present hope of solution. Consumption may have been known to the Egyptian physicians who were entrusted with the embalming of the dead, and references in the Bible (Leviticus, 26:16, and Deuteronomy, 28:22), written about B.C. 1500, indicate that it was this disease which Moses pronounced as a curse to be visited for disobedience. Commentators consider the original meaning of the passages to have included various wasting disorders. It is also evident that the laws recorded in the Talmud (Mischna, B.C. 500) indicated the recognition of tuberculosis in cattle, and forbade the use of diseased animals in which ulcers existed.

Hippocrates (B.C. 460–376) was the first to give an intelligent description of phthisis, although empyema and "phyma," abscess of the lung, were included in his classification. Otherwise his portrayal of the symptoms of consumption was unsurpassed for many centuries, and his works became classic. The etiology of phthisis, according to Hippocrates and other early writers, was principally the irritation of the lungs caused by the "flux" or mucus of the body flowing from the head into the air passages and causing ulceration by its retention in the bronchi. The Hippocratic school believed in the curability of phthisis in all stages and the benefits of a change of residence. Contagion was mentioned by Isocrates. Aristotle, also a contemporary of Hippocrates, notes that it was a general belief among the Greeks of his day that phthisis was contagious. Celsus (B.C. 30) wrote of the disease in three forms: atrophy, cachexia, and ulceration. Aretaeus (A.D. 50) gave a very clear description of the disease and differentiated it from empyema. He believed in the efficacy of sea voyages and country air. Pliny also lauded pine forests for their healing powers.

[1] The writer is indebted for much of the history and chronology in this chapter to the works of Waldenburg, *Die Tuberkulose*, 1869; also that of Predöhl, *Die Geschichte der Tuberkulose*, 1888, and Johne, *Die Geschichte der Tuberkulose des Rindes*, etc., 1883.

Galen (A.D. 131–201) considered the disease an ulceration which should be treated by measures designed to dry the secretion. He therefore sent patients to the high land of Phrygia. In other details the conceptions of the disease held by Galen were like those of Hippocrates; nor was any further light shed upon the nature of consumption for 1400 years, when anatomical study began.

**From Sylvius to Laennec.**—The celebrated Sylvius (1695) was the first to indicate the connection between tuberculous nodules and phthisis. He regarded these nodules as enlarged lymph glands in the lung, analogous to scrofula, and on the scrofulous constitution depended the inheritance of phthisis. True phthisis always meant lung ulceration, and depended on two chief causes, which may be expressed as constitutional and local, the first affecting the nutrition of the lung, the second causing the ulcerations. He gave a careful description of the symptoms, and believed in contagion. Willis (1622–1675) would not accept the teaching that phthisis arose from the secretions of the head, and disputed the connection between ulcus pulmonum and phthisis. Bonnet (1620–1689), who made more than 150 sections, published observations, among which were cases of obvious miliary tuberculosis, but made no careful distinction between lung affections. Manget (1700), who revised Bonnet's work and added his own investigations, first likened miliary tubercles to millet seed, and described them in organs other than the lungs. He also mentions the caseation and softening of the lung tubercles, the latter of which he considered to be of scrofulous nature.

Morton (1689), whose celebrated book was widely known among English physicians, brought the tubercle prominently to attention as the true cause of phthisis; tubercles were either benign or malignant and due to obstructed glands in the lung from excess of lime in the lymph or hypersecretion causing stagnation and hardening. He described fifteen kinds of consumption, of which the scrofulous was the most important; he also believed in heredity and contagion. Morgagni (1682–1771) was uncertain that tubercles and glands were identical, and thought that phthisis could originate from other things; he regarded it as extremely infectious, and refrained from doing autopsies on consumptives.

The noted Sydenham (1624–1689), Boerhaave (1668–1738), and his pupils Auenbrugger and Van Swieten, wrote of phthisis without adding anything of importance to the previous conceptions of its nature, but largely represented the views of Hippocrates, Galen, Sylvius, and Morton. Mention should be made of Cullen (1800), the celebrated Scotch teacher, under whom Benjamin Rush, of Philadelphia, studied. Cullen wrote a celebrated treatise on phthisis, but did not emphasize the tubercle or its contagiousness; scrofulous glands in the lungs were the antecedent of phthisis to him. The teachings of Benjamin Rush exerted a powerful influence on American medicine of Revolutionary times. He wrote *Thoughts upon the Causes and Cure of Pulmonary Consumption* (1783), in which it was regarded as a disease of debility and tubercles the result of hypersecretion from the bronchial vessels. He believed in contagion at first, but doubted it in later life. His treatment was vigorously antiphlogistic: bleeding, purging, etc., in the acute or febrile stages, and supporting measures in the debilitated stages.[1]

[1] H. B. Jacobs has presented an excellent account of Benjamin Rush and other American writers on tuberculosis in *Johns Hopkins Hospital Bulletin*, 1902, vol. xiii.

A definite advance came in the latter part of the eighteenth and beginning of the nineteenth centuries, when Stark (1785) accurately described miliary tubercles and prepared the way for the correct understanding of their nature and relation to phthisis. Reid (1785), who edited Stark's work, considered the glandular or scrofulous nature of tubercles questionable.

Kortum (1790), Baume (1795), and Hufeland (1796) held substantially the same opinions as Cullen. An important contemporary work by Baillie (1793) carried the knowledge of tubercles beyond that of Stark. He recognized the transition stage of tubercles from small to large by coalescence and then to softening. He was the first to recognize the tubercles in other organs than the lung, but called them scrofulous. Portal (1780) coincided with Baillie generally and disbelieved in infection, but introduced confusion by naming all caseous material "tuberculous." Vetter (1803) also confirmed Baillie's results by independent studies.

Most noteworthy is the work of Bayle (1803), who is justly named by Waldenburg as the founder of the correct teaching about tuberculosis. He studied miliary tubercles in all stages and laid stress on their varying degrees of opacity; earlier gray tubercles were "granulations" of quite different character. True tuberculosis was a constitutional affection which can cause the development of nodules in all the organs and not originate in inflammation, although often complicated with it; it depended upon the "tuberculous diathesis," and was of scrofulous nature. There were six kinds and the three classic stages of progress described.

**From Laennec to Villemin.**—Laennec (1819), whose work soon followed Bayle's, consummated and simplified the knowledge thus far gained. He recognized the unity of all phthisis as tuberculosis and scrofula as tuberculosis of lymph glands; his ideas in general as to causation and infection were distinctly modern, and his descriptions of the tubercle and its transformation toward ulceration are unexcelled. Most valuable of all was his gift of the art of auscultation. No genius like that of Laennec so far anticipated his own day.

The teachings of Bayle and Laennec were not accepted without opposition. Broussais (1816), who attributed most chronic diseases to inflammation, viewed phthisis as a chronic pneumonia. Bichat (1823) inclined to the same theory. Gendrin (1828) held that serous membrane "granulations" were different from actual tubercles. Magendie (1821) and Andral (1829) introduced the theory of tubercle as a secretion product and regarded caseation as inspissated pus; an inherited predisposition as well as active inflammation was needed to induce tubercles. Louis (1825) established Laennec's teaching, but returned to the idea that the small, gray granulations were not tuberculous until caseated. He was the first to make a scale of the incidence of phthisis in the different life periods.

During this period America was represented but meagerly in original investigation until 1834, when Samuel Morton, of Philadelphia, published the first pathological studies on consumption. He was a student of Laennec, and his conclusions as to the nature of tubercles were fairly accurate; they were ascribed to altered secretion and not to inflammation. Morton's work on *Pulmonary Consumption* found much favor in America, and included excellent therapeutic advice as to open-air life and exercise.

**Inoculation Experiments.**—During the period of pathological study at the end of the eighteenth century the subject of the infectiousness of phthisis

excited some attempts at experimental inoculation. The belief in contagion was universal, but in varying degree. English, American, and German physicians accepted the probability of infection under special conditions, but the strongest opinions were held by the Latin races, among whom the disease was said to be more virulent. The influence of Valsalva and Morgagni was certainly most potent in causing fear in Italy.

The first recorded inoculations were by Kortum (1789), which, like those of some of his successors (Lepelletier, 1830; Goodlad and Deygallières, 1829), were fortunately unsuccessful, since they were partly upon human beings, including themselves. The strife over the question of the danger of inoculation of scrofula with vaccination led to these first attempts. Klencke (1843) first announced successful intravenous inoculation of a rabbit. Meanwhile, other experiments with quicksilver (Gaspard, 1812; Cruveilhier, 1826; Lombard), with glanders (Schilling, 1822), and others, whereby tubercle-like nodules were produced, led opinions astray as to a specific character in tubercle; so that Klencke's observation was apparently without effect. Great attention was bestowed upon the microscopic and chemical investigations during the first half of the nineteenth century, owing to the improved instruments and methods, and hypotheses multiplied about tuberculosis, based on the result of these studies. Some of them may profitably be enumerated here. Tuberculosis was regarded as a fibrous exudate due to a special dyscrasia by Rokitansky (1842), who was the first to record the microscopic appearance of the tubercles. Vogel (1845) also considered tubercles as fluid exudates. Engel (1844) believed the cause to be the same as typhoid, only the dyscrasia caused a different exudate. Escherich (1845) emphasized the influence of soil. Eichmann (1845), changes in the sympathetic nerve. Furnivall (1842) attributed it to deficient innervation. Dupuy (1817) and Baron (1822) to hydatids. In England tuberculosis was ascribed to scrofula, which in turn was due to an unknown cachexia, Alison (1824); Glover (1847); Simon (1850); Carswell (1843), and James Clark (1836).

The theory of Addison (1843) that tubercles originated from leukocytes caught in capillaries and transformed into abnormal epithelial cells was interesting. The studies of Lebert (1849) evolved a claim for a peculiar cell associated with tubercle which he called the "tubercle corpuscle." This was refuted by Henle (1847) and Reinhardt (1850), who found them in ordinary pus. Virchow (1847–50) classed scrofula and tuberculosis entirely apart, restricting the latter term to the miliary form and considering it a form of lymphoma due to an unknown diathesis; caseation was a non-specific process. Hence the idea of unity in tuberculous diseases received a serious rebuff in spite of the important discovery by Buhl (1857) that miliary tubercles were most often associated with preëxisting caseous foci, from which he thought the specific poison originated. The microscopic studies had brought out valuable data, but withal much confusion of ideas.

The chemical analyses of tuberculous tissue, especially of cheesy material, had brought no better result, and the epoch-making experiments of Villemin could not have been better timed.

**Period from Villemin to Koch.**—Villemin presented his important communication in December, 1865, "On the Cause and Nature of Tuberculosis and the Inoculation of the Same from Man to Rabbit." His conclusions

were positive: "(1) Tuberculosis is a specific affection. (2) It has its origin in an inoculable agent. (3) The inoculation from man to rabbits is very successful. (4) Tuberculosis pertains, therefore, to the virulent diseases, and should be classed with variola, scarlatina, syphilis, or, better still, with glanders." He covered a wide field in his inoculations, employing fragments of lung tubercle, sputum, blood, scrofulous gland, and perlsucht or bovine tubercle, with positive results in nearly all cases. He failed to infect sheep, goats, and birds, and thought them probably immune; later experiments on dogs and cats showed only relative immunity in the carnivora. His control experiments with cholera dejections, pus from glanders, cancer masses, worm nodules, and pneumonic lung were all negative. Therefore, while there was nothing specific in the structure of the tubercle or in caseation, true tuberculosis was always inoculable; this was the only test for Villemin. Scrofula was not invariably tuberculous, because not always infective. Villemin's conclusions excited widespread discussion and control experimentation, for such far-reaching statements commanded attention.

A new era of science was founded about the same time by Pasteur, and had not he become engaged in other investigations it is permissible to think that his genius might have crowned the work of Villemin by anticipating Koch's discovery by several years. It was not without great turmoil and strife of opinions that the truth finally emerged, for the contradictory results of inoculations were difficult to interpret. Every conceivable method of inoculation in control experiments was used. Besides tuberculous products there were those of cancer, syphilis, typhoid, pneumonia, and suppurations; inorganic substances, such as cinnabar, glass, silica, coal-dust; organic material, filter paper, hair, cork powder, lycopodium seeds, croton oil, moulds, etc. Coincidently exhaustive histological studies were carried out and their results discussed with fervor. The majority of experimenters corroborated Villemin's results in part, but much weight was brought against his conclusions about the specificity of tubercles by those who obtained tubercle-like nodules from indifferent substances. The old idea of inflammation dominated many, who regarded tuberculosis as simply a reaction to many kinds of irritation. Lebert, Andrew Clark, Cohnheim and B. Fränkel, Aufrecht, Wilson Fox, and Waldenburg were prominent among the opponents of specificity. The inhalation experiments of Schüller (1877), Tappeiner (1878), the eye inoculations of Langhans (1868), Cohnheim and Salmonsen (1877), Baumgarten (1880), and the feeding and other experiments of Klebs, Chaveau (1873), Bollinger (1873), together with the accurate histological studies, gradually restored the belief in a specific virus common to human and bovine species.

The contest over the specificity of the giant cell, the importance of which was emphasized by Langhans (1868), was settled in the negative. Tubercles were studied in all the tissues hitherto unassociated with the conception of tuberculosis, as fungous joints, carious bones, and lupus, by Koster (1873) and Friedländer (1873). The development and spread of miliary tubercles were traced to venous infection by Weigert (1879–82). The pathway of infection was already inferred by the many feeding and inhalation experiments, so that with the rapidly developing investigation of bacteria caused by Pasteur's discoveries search was being made for a specific living organism. E. Klebs (1877) was the first to observe actual trans-

ference of the virus by artificial culture on egg albumen through several generations before inoculation, but he did not succeed in recognizing the bacillus; instead he found a motile organism, the *Monas tuberculosum*, which he presumed to be the *contagium vivum*. Schüller (1879), Reinstadler (1879), and Touissant (1881) also succeeded in cultivating the still unknown virus. Aufrecht (1881) and Baumgarten (1882), independent of Koch, described bacilli in the centre of the tubercles, which, owing to lack of culture and staining methods, were not positively identified as the infective agents. Thus the actual achievement was due to Robert Koch, who was a health officer in an obscure German town.

Koch's demonstration of the causative relation of the tubercle bacillus to tuberculosis was so complete that but little of importance has been added since. The first attempts at staining the organism were by means of methylene blue made faintly alkaline by caustic potash and with vesuvin as a contrast stain. With these stains Koch was able to demonstrate the bacillus in all kinds of tuberculous tissues of man and animals, except when the tubercles were calcareous or otherwise healed. Moreover, by cultures on blood serum through several generations and re-inoculation the proof was made complete, and the long dispute about the nature of scrofulous gland and skin diseases as well as various pneumonias was finally settled. It is true that skeptics and experimenters with faulty methods continued to arise and cast doubt upon the truth, but they gradually disappeared. Nevertheless the logical application of the knowledge, so conclusive and simple as to the infectiousness of sputum, has required many years to become general. Much aid was given in this direction by the investigations of Cornet (1888) on the presence of bacilli in dust.

The subsequent announcement of tuberculin as a probable cure (1890), the more recent discussion as to the relationship between human and bovine tuberculosis excited by Koch (1901), the vaccination studies, and the still more radical views introduced by v. Behring (1902) as to the source, time, and pathway of infection, constitute periods in the recent history of tuberculosis to which may be added the rapid extension of preventive measures and the sanatorium movement.

## ETIOLOGY.

**Statistics.—General Statistics.**—The prevalence of tuberculosis is universal; no other disease is so widespread or produces so much poverty and long-continued distress. Mortality tables do not convey a tithe of the number actually infected as revealed by pathological examinations, yet even such figures as are obtainable from death and census returns show an appalling annual sacrifice. From one-seventh to one-tenth of all deaths and an enormous proportion of invalidism are due to it. Kayserling stated at the recent Paris Tuberculosis Congress (1905) that one-third of all deaths and one-half the sickness among adults in Germany can be charged to tuberculosis. A. Newsholme states that 11.3 per cent. of all deaths in England and Wales are still due to it. The last *United States Census* (1900) gives a total of 111,059 deaths from consumption, including general tuberculosis, the rate being 109.9 per 1000 deaths, or about one-ninth of the deaths from all known causes. Other forms of tuberculosis and deaths from intercurrent

diseases in the course of consumption do not appear in the last-mentioned statistics, so that the true figures are appreciably greater.[1]

The following are the totals for the year 1900 in two countries:

| | Population. | Cases. |
|---|---|---|
| United States | 76,000,000 | 111,059 |
| German Empire | 56,000,000 | 118,706 |
| Total | 132,000,000 | 229,765 |

The lack of uniform systems of registrations of deaths makes a comparison of various countries and states imperfect at best. The important factors influencing the mortality tables are density of population, occupation, social condition, race, color, and sex. Quoting from the *United States Census*, 1900, Part I: "The death rate from consumption was about the same in the cities in the registration States (204.8 per 100,000 population) as in the cities in the non-registration States (204.9), in both of which it was much higher than in the rural districts of the registration States (134.1). The death rate of the colored race from consumption (490.6) was nearly three times that of the whites (173.5), and that of the foreign whites (231.1) was much higher than that of the native whites (155.4). For the last-mentioned class the death rate for those having one or both parents foreign (184.8) was also much higher than those of native parents (126.5). The death rate of males from this disease (white 188.3, colored 527.3, including Indians and Chinese) was considerably higher than those of females (white 158.8; colored 455.1)." As to the last statement the reverse is true in the country as a whole, the female rate being higher in the rural districts.

Occupation and social condition appear to have the most intimate relation to the ratio of mortality. Stonecutters, cigarmakers, and plasterers head the list with about half the deaths in these occupations; farmers and persons under the best social conditions have less than one-eighth due to tuberculosis. The greatest mortality from tuberculosis is between the fifteenth and forty-fourth year of life, when it causes one-third of all the deaths occurring during that period. The months of greatest mortality are March, April, and May, when other respiratory diseases are at their height.

The economic loss from tuberculosis is enormous even with a low valuation placed upon an individual life. Taking an average of $500 as the earning power during the most productive years, the cost to the United States for the year 1900 was approximately $45,000,000, there being 89,305 deaths between the ages of fifteen and sixty, or more than four-fifths of the entire number. In the German Empire there were 85,280 deaths in the same year. Estimating the loss of earnings according to Cornet at 600 marks per annum, the sum was 51,168,000 marks. When it is recalled that the average time of partial or complete disability of a consumptive is at least two years, and the enormous cost of nursing and support has not been included, the above sums may be trebled with fairness. Biggs estimates the cost to New York City alone as $23,000,000. It is safe to say that tuberculosis costs the United States $150,000,000 to $200,000,000 yearly.

[1] In the United States 88.5 per cent. of the tuberculosis mortality (1900–1904) in the registration area was classified as "tuberculosis of the lungs." A. Newsholme gives 69 per cent. for England and Wales (1903), Cornet 81 3 per cent. for the German Empire (1896 to 1900).

**Geographical Distribution.**—Tuberculosis is prevalent at all latitudes and altitudes and in all climates. It is most frequent in temperate zones and lowlands and is rare in the elevated plateaux and Arctic regions. The influence of occupation and density of population explain to a large extent the differences in its incidence rather than geographical location alone. There seems, nevertheless, to be a distinctly protective influence in the climates of arid regions, and especially in elevated, invigorating climates, as Colorado, Mexico, and the Alps. The tropical countries furnish no statistics as to the frequency of tuberculosis, but it is said to be less common than in temperate regions, although more rapid in its course. In Natal, South Africa, the disease is infrequent according to J. F. Allen.[1] Prinzing[2] has made a comparative study of the death rate to emphasize the relatively greater importance of other factors than geographical situation. For example, the average tuberculosis mortality for the year 1891 to 1900 in Switzerland was 26.1 to 10,000, while in England it was 20.1, but in Ireland 27.8. Likewise in Germany the rate was 24, but in Austria 34.5 and in Hungary 36.4.

**Race.**—The question of varying susceptibility in different races has been much discussed and is closely connected with that of inherited or acquired immunity. It is certain that the aboriginal and uncivilized peoples easily acquire it in a rapidly fatal form, even when their conditions of living are favorable. Notable among such races are the American Indians, Negroes, and Hawaiian Islanders. The so-called half-breeds and mulattoes are especially liable to the disease, and it has usually followed the advent of the white races among uncivilized natives. Benjamin Rush stated that the disease was unknown in America among the Indians in their natural wild state, but the early New England physicians mention its prevalence among the natives in their day. The recent emigration to Alaska has been followed by the decimation of the Indians from various diseases, especially measles and tuberculosis in acute forms. It is reasonable to suppose that the greater virulence is in part due to greater susceptibility of tissue, though undeniably the chief factors are filthy habits, poverty, and predisposing diseases. The mortality from consumption in recently immigrated races in the United States is generally much higher than those of longer residence. Among those whose mothers were of foreign birth the rate was highest in the Irish (339.6); French (187.7); Scotch (172.5); Germans (167); while the rate was lower (71.8) in the Russians, Poles (107.7), and in the Hungarians and Bohemians than in the natives of the United States (112.8). That this different mortality is due to varying susceptibility is very doubtful. On the other hand, the Hebrews are thought to have relative immunity to tuberculosis.

**Decrease of Tuberculosis.**—One of the most encouraging and instructive facts is the remarkable decrease in the death rate in civilized countries during the last fifteen years. It is at once a confirmation of the value of the hygienic measures and one of the obvious benefits of improved conditions of life for the laboring classes in large cities. From being the greatest scourge during the nineteenth century, when Good thought it no exaggeration to estimate that one-fourth of the population of Europe died of consumption, it is becoming so greatly lessened that in twenty years, from 1885 to 1903, the rate for Prussia fell nearly one-half, or 3.1 to 1.9 per 1000 living. (Kayserling.)

[1] *Transactions of the British Congress for Tuberculosis*, 1901, vol. iii.
[2] *Zeitsch. f. Hygiene u. Infek.*, 1904, vol. xlvi.

The same is true of England, where a decrease of 50 per cent. has taken place in forty years. In the United States there was a decrease of 54.9 per 100,000 living between 1890 and 1900, the rate being 254.4 and 109.5, respectively. This decrease is principally in the large cities, New York being the most conspicuous by a lessening of 40 per cent. in 16 years (4.06 to 2.68 per 1000, 1887 to 1902). "During the last ten years there has been a decrease of 40 per cent. in the death rate from pulmonary tuberculosis and tuberculous meningitis in children under fifteen years. It is precisely in the youngest element of the population that one would first look for definite results from the enforcement of measures for the restriction of the diseases" (Biggs). Massachusetts has exhibited a marvellous decrease of over 50 per cent. (7.77 to 3.1) in the fifty-one years between 1851 and 1902. The decrease has steadily continued in all the Eastern and Middle States and to a considerable extent in the rest of the country. In five of the New England cities the death rates decreased from 30.7 to 21.4, and in seven of the Middle States cities from 31.4 to 23.4 per 1000 population. The latest mortality reports (1906) from the United States registration cities bring the average per 100,000 from 1900 to 1904 to 190.3, as compared with 204.8 in 1900 and 265.6 in 1890.

In some foreign countries the decrease is less marked during twenty years, but yet distinctly evident, as in London (3.12 to 2.34), Berlin (3.6 to 2.39), and Vienna (7.2 to 4.76). No decrease has occurred in Paris to 1900, where the rate was very high (5.46). A. Newsholme,[1] who has made exhaustive studies, finds that the factors accompanying the decrease are very complex, and that much of the decrease had occurred before the discovery of the tubercle bacillus and the increased hospital and sanatorium care; the latter, however, he considers the most important factor: "Segregation in general institutions is the only factor which has varied constantly with the phthisis death rate in the countries that have been examined. It must therefore be regarded as having exerted a more powerful influence on the prevention of phthisis than any of the other factors of which none has varied constantly with the phthisis death rate."

To summarize the facts: (*a*) The death rate from tuberculosis has decreased, in the places where special attention has been given to the hygienic control of the disease, from one-seventh of all deaths in 1890 to one-tenth in 1900. (*b*) The general mortality from all diseases registered has declined from 19.6 to 16.7 per 1000 in the United States between 1890 and 1904, principally because of the lessened rates from tuberculosis and children's diseases. It is significant that the development of sanitation has been rapid during this decade.

**Zoological Distribution.**—*Animals in Natural State.*—Tuberculosis is practically unknown in animals or birds in the wild state or among those who have never been confined or brought in contact with domesticated species. Cattle who roam wild upon the plains are very rarely found to be affected. In abattoirs the number for all the cattle inspected, coming chiefly from the plains, was but 0.134 per cent. in 28,000,000.[2] It is quite otherwise with animals in menageries and zoölogical gardens; here the disease is

[1] *Journal of Hygiene*, 1906, vol. vi, p. 374.

[2] *United States Bureau of Animal Industry Reports*, Postmortem Inspection, 1900 to 1905.

frequent among a great variety of herbivora, but less often among carnivora, in whom it is also more chronic in character. Monkeys and apes are the chief sufferers; rabbits and guinea-pigs rarely acquire it spontaneously. Instances are known of the disease in the giraffe, antelope, zebra, lion, tiger, jaguar, panther, fox, jackal, tapir, etc. Wild birds in aviaries are likewise subject to avian tuberculosis, but, excepting parrots, rarely acquire the mammalian type. Occasionally, carnivorous birds like the hawk, eagle, owl, and stork have been found tuberculous, as well as water fowl—ducks, geese, swans, and cranes (Nocard, Woods Hutchinson, Weber and Taute, Rabinowitsch). Spontaneous tuberculosis in reptiles, fishes, and other cold-blooded animals has been long regarded as a possibility, though rare. Inoculation experiments with mammalian tubercle bacilli also seemed to confirm this opinion, but more careful recent investigations (Weber and Taute 1903) have revealed that the disease in these animals is probably a form of pseudotuberculosis produced by a saprophytic bacillus.

*Domestic Animals.*—All domesticated animals and birds are known to be liable to tuberculosis, but the frequency is greatest in dairy cattle. The proportion is estimated as from 10 to 15 per cent. in America, but is much greater in the British Isles and Europe, where as high as 30 per cent. has been discovered by inspection and the tuberculin test. It is said to be unknown on the islands of Jersey and Guernsey; also in Japan, where a certain insusceptibility appears to exist among the native stock (Kitasato). The greater incidence of tuberculosis among highly bred cattle is significant of the effect of more careful housing and hence greater opportunity for contagion. The increasing use of the tuberculin test has revealed an enormous prevalence of latent tuberculosis in apparently healthy cows. Next in frequency to dairy cattle, hogs are most subject to this disease and suffer chiefly from the bovine type of tubercle, from which fact it is evident that they obtain the infection from cattle, both by association and in food, especially milk. The practice of feeding offal obtained from abattoirs is a frequent source of infection. The *United States Reports of Inspection* show 0.23 per cent. in 119,000,000 hogs slaughtered during 1900 to 1905, but it is more frequent in Europe.[1] The disease in hogs is often acute, but also presents a chronic lymphatic type; hence the name "scrofula," from *scrofa*, a sow.

Sheep are seldom affected, there being but 0.003 per cent. in 37,000,000 inspections, many of which were probably instances of pseudotuberculosis. Horses are rarely attacked, only one instance in 9544 inspections being reported. Nocard mentions having seen eleven cases of abdominal tuberculosis in horses, which were evidently derived from intestinal infection of bovine origin. Goats and asses are likewise relatively immune to spontaneous infection, but European veterinarians have reported several cases among goats. Camels are occasionally tuberculous. Dogs and cats, like other carnivora, are quite insusceptible, yet several hundred cases have been recorded, and the disease is acquired by contact with consumptives, in most instances from swallowing or inhaling sputum. Kittens are quite easily infected from milk containing tubercle bacilli (Nocard). Among rodents, rats and mice are highly resistant to experimental tuberculosis and

[1] The *United States Report* for the year 1905 shows a large increase in hogs, which reached about 3 per cent. in the largest abattoirs, and is to be made the subject of special inquiry.

are not spontaneously diseased. On the other hand, rabbits, guinea-pigs, and gophers are readily inoculated, yet seldom acquire it even in confinement.

Avian or fowl tuberculosis is most frequent among chickens, in whom it may become epidemic when once introduced into a flock. It seems to be common in Europe, but relatively infrequent in America. Pigeons, turkeys, ducks, geese, and pheasants have it to some extent, by reason of their habit of feeding with chickens whose infected excreta contaminates the food. Cases among canaries and other small pets are recorded, but more often parrots have obtained the disease from human sputum by accidental inoculation.

**Bacillus Tuberculosis.—Morphology.**—The tubercle bacillus is a minute, colorless rod, and according to the classical description of Koch has a slightly bent shape, with generally uniform contour and slightly rounded ends. It is very variable in length and somewhat so in thickness. The forms usually found in sputum vary in length from 0.0015 to 0.004 millimeter (1.5 to 4 $\mu$), from one-fourth to one-half the diameter of a red blood cell and in diameter about one-fifth the length of the rods.

*Staining Properties.*—The most striking peculiarity which distinguishes it from most other bacteria is the power to hold aniline dyes in spite of long exposure to acids and alcohol. The exceptions which may cause confusion are few: the smegma and the probably identical so-called syphilis bacillus; the leprosy and the various pseudotuberculosis bacilli. The acid-alcohol resistance is due to the peculiar waxy nature of the bacillus, which substance by extraction with alcohol and ether may be entirely removed, and with it the specific staining reaction. Ordinary basic aniline dyes stain this organism with difficulty.

*Pleomorphism* and *Classification.*—The many modifications in form and size which can be produced by varying the growth conditions have led bacteriologists to class the tubercle bacillus as a parasitic fungus capable of a higher order of development than ordinary bacteria. The observations of Roux, Metchnikoff, Maffucci, Klein, Fischel, Coppen-Jones, Craig, Abbot and Gildersleeve, Wolbach and Ernst, and others have conclusively shown that under favoring conditions for saprophytic growth, bizarre forms with lateral branches and long filaments with club-shaped ends or swellings and vacuoles may appear, of a striking similarity to actinomyces. This pleomorphism of tubercle bacilli is rarely found in the true parasitic condition of growth, *i. e.*, in the tissues of animals, but may be found in sputum, where they are probably evidences of growth on the inner surfaces of lung cavities. Coppen-Jones, Lubarsch, Friedrichs, and Schulze have also observed the club forms and fungus-like radiate arrangement in tubercles of rabbits inoculated with human, avian, and pseudotubercle bacilli. These branched forms and other morphological variations are most often found in cultures of fowl tuberculosis, but also in those of human and bovine types (Wolbach and Ernst).

The more easily a particular strain of bacilli may be artificially cultivated, and the longer it has thus grown as a saprophyte, the more frequently it assumes the irregular forms. In consideration of these similarities to other fungi, bacteriologists are inclined to place the tubercle bacillus in a class intermediate between the bacteria and streptothrices; hence the name proposed by Coppen-Jones, "tuberculomyces," and by Marpmann, "mycobacterium tuberculosis."

*Spore Formation and Involution Forms.*—Koch described highly refracting bodies in the tubercle bacillus, most of which took no stain, but some were intensely stained and unusually resistant to acids. He considered both to be evidences of spore formation, but the unstained segments familiarly known in many sputum bacilli have since been recognized as vacuoles or breaks in the protoplasm. The globular, deeply staining bodies are, however, more nearly allied to spores, though not possessing the heat-resisting powers of other known spores. They often occupy one end or the middle of a bacillus, and the deeply stained balls with a faintly stained rod attached, which is usually of lesser diameter, are very characteristic for old or inactive cultures. They are also seen in considerable numbers in sputum from chronic cases. All the bacilli may show them, and the conclusion is justified that they are resting forms even if not strictly signs of sporulation. They resist drying longer and are found in dust specimens (Coppen-Jones). It is possible also to produce forms resembling them by overheating a slide specimen. Degeneration forms of tubercle bacilli are often seen together with the nodulated bacilli. The vacuolation is due to shrinkage and loss of protoplasm, which then loses more or less of the acid resistance in decolorized preparations of old or dead bacilli. Young living cultures may occasionally present vacuolation when cultivated on brain media (Wolbach and Ernst). In the main, however, young forms do not have many vacuoles in ordinary cultures, nor in sputum from acutely progressive disease. They may readily be produced in an artificial way by extraction with solvents.

**Varieties.**—At the present time it may be stated that there are four fairly distinct types of strictly infectious tubercle bacilli: the human, bovine, avian, and reptilian or piscine. Besides these there are certain saprophytic bacilli which are probably distinctly related to the preceding and properly classed as pseudotuberculosis bacilli. All four parasitic forms of tubercle bacilli have certain characteristics in common, but are sufficiently variable in others to be distinguished from each other. Many observations in the past tended to show that these varieties were mainly accounted for by differences in the host which harbored them, being capable of comparatively rapid transformation one into another and originating from a common source or stock. This, in fact, was the original belief of Koch at the time of his first inoculation experiments, but the studies on the morphology and virulence of mammalian bacilli by Theobald Smith (1898) and those of Lartigau, Ravenel, Schutz, and others raised doubts as to their identity and to disputes as to the inter-inoculability of the human and bovine types. The constancy of these differences led Koch to a negative position as to the danger of "perlsucht" or bovine tubercle bacilli for man, and to a diligent study of the whole question since the discussion at the British Congress for Tuberculosis (1901). Out of much strife the truth seems to be emerging in favor of an intermediate position between the standpoint of those who hold the belief in strictly distinct varieties and those who favor an absolute unity for all. While the German Imperial Commission[1] appointed to study the question has reported in favor of radical distinctions as held by Theobald Smith, the United States Bureau of Animal Industry[2] finds that the types of tubercle bacilli are very

[1] Kossel, Weber, Heuss, Taute, and Beck: *Tuberculose Arbeiten aus dem Kaiserliche Gesundheitsamte*, vol. i, 3.

[2] De Schweinitz, Dorset, Schroeder, and Cotton: *United States Bureau of Animal Industry*, Bulletin No. 52, I–III.

inconstant. The conclusion of v. Behring that varying types and transition forms depend solely upon the animal host, and that the virulence of a given strain of bacilli furnishes no criterion as to its original source, is practically concurred in by the British Royal Commisson on Tuberculosis,[1] whose report of extensive experiments with bovine and human cultures speaks for the essential unity of these two forms. Nevertheless, while the main point of contention, namely, that the bovine type of bacilli is capable of infecting human beings, is now considered settled affirmatively, there is yet sufficient reason for a broad distinction between the human and bovine types, and still more between them and the avian and reptilian bacilli. It is therefore important to note the points of difference possessed by the most characteristic individuals in each class.

*Human Type.*—This form, already described above, has a greater length (2 to 2.5 $\mu$) than the bovine, and is thinner and more regular in outline and staining, but is less easily to be distinguished microscopically from the avian type. It grows more readily on all media, produces increased acidity in culture broth (Smith), and is less virulent for small and large herbivora than the bovine. It rarely infects carnivora, and yet more rarely fowls, birds, and reptiles.

*Bovine Type.*—The average length is from 1 to 1.5 $\mu$. In comparison with the longer human and avian types the outline is more irregular and often oval and plump with blunt ends; the staining is less uniform, but vacuolation is not so evident. The growth is slower in cultures, though ultimately not different in appearance from the human and produces an alkaline reaction in culture broth (Smith). It is infectious for all mammals so far tested by inoculation experiments, and is more virulent for them than the human type. It has been found in the mesenteric and cervical nodes of human beings, and in the sputum at least once. Its infectiousness for fowls has been open to doubt (Weber and Bofinger), although v. Behring reports an instance of spontaneous infection in chickens from which he isolated bacilli virulent for cattle.

*Avian Type.*—The bacillus of chicken tuberculosis is similar to the human type in general appearances, but shows pleomorphism more frequently. The rods are often more slender and longer than the other varieties, and much less adherent to each other in growth; therefore, they do not form the compact masses seen in stained smears of the human and bovine types. Growth is rapid on all media and is distinguished by a moist, creamy consistence seldom seen in the others; it thrives at a higher temperature (43° C.) and produces an alkaline reaction in broth cultures (Bang). It is highly infectious for barn-yard fowls, but less so for pigeons and carnivorous birds. Very few animals are susceptible and guinea-pigs are nearly immune. Rabbits may easily be infected. Mice, rats, and pigs have been successfully inoculated and have been found spontaneously diseased (Rabinowitsch), but the larger animals are quite refractory; it was, however, found in a monkey by Rabinowitsch. Cases have also been reported where the avian bacillus has been found in human sputum (Kruse, Pansini, Rabinowitsch) and in intestinal tuberculosis in cattle and horses (Johne and Frothingham, Nocard), but they lack complete proof of their origin from avian sources.

[1] *Second Interim Report of the Royal Commission*, etc., 1907, Part II, Appendix, vol. iv.

*Reptilian and Piscine Type.*—It has been customary to include among tubercle bacilli certain varieties which grow readily at low temperatures (20° to 25° C.), and are found in fishes and cold-blooded animals, such as frogs, snakes, lizards, and turtles. These are now relegated to a class by themselves and are only infectious to reptiles and fishes under unknown conditions, but not to mammals and birds so far as known. The studies of Weber and Taute have apparently shown that they belong to the class of pseudotubercle bacilli which can grow in nature as saprophytes and cannot be ascribed to an alteration of mammalian or avian types under natural conditions.[1]

*Pseudotubercle Bacilli.*—During recent years an increasing number (between 30 and 40) of acid-proof bacilli have been encountered which strongly resemble true tubercle bacilli in morphology and staining properties, but more often show actinomyces-like forms. The most important are the milk and hay bacilli of Moeller and the butter bacilli of Rabinowitsch, Petri, and others. They are generally rather thicker and less acid-proof than true tubercle bacilli, and all grow more rapidly and at low temperatures. Cultures of the various milk, pseudobovine, and grass bacilli, of which many varieties have been described, are similar in so many features that it is very likely that they are closely related if not identical in origin. Some form yellowish-red pigment in mature cultures, but otherwise much resemble tubercle bacillus growths.

The smegma group forms another series of acid-proof bacilli which are of more importance in causing confusion in the diagnosis of tuberculosis. They are found about the external orifices of both man and the lower animals, and there is evidence to show that the presence of sebaceous fat at these situations has much to do with their resistance to decolorization.

The reptilian bacillus cultures are more like the avian in their soft, creamy consistence, and practically indistinguishable from mammalian and avian types in stained specimens. None of this class can claim parasitic importance for mammals, yet inoculation may produce localized tubercles which soon disappear without caseation in guinea-pigs and rabbits, thereby indicating that they are like the result of any foreign body irritation.[2]

No evidence has been forthcoming that any spontaneous disease results from these organisms except in fishes and reptiles (Dubard, Friedmann, and Küster).[3] They have been a source of error in some of the earlier researches in connection with milk and butter; nor can they be neglected in connection with the diagnosis of human tuberculosis, especially of the genito-urinary and intestinal tracts. They have been found in cases of lung abscess and

[1] The fish bacillus of Bataillon, Terre, and Dubard, the blind-worm bacillus of Moeller obtained from a worm inoculated with sputum, and the turtle bacillus of Friedmann are forms supposed to have been produced by the alteration of mammalian types. Sorgo and Suess (Cf. *Bakt.*, vol. liii) also found this true in their inoculation experiments with cultures of human bacilli on snakes and worms, in which they produced tubercles and apparent infection.

[2] An exception appears in the *Bacillus tuberculoides II* (Beck), which has the morphology and staining peculiarities of the pseudotubercle bacilli, but the actual position of which is not yet certainly with that class, since it is infectious for guinea-pigs, rabbits, and white rats, and was isolated from the tonsil of a consumptive woman. It may be an intermediate variety between the pseudobacillus and true human bacillus, but in rapidity of growth resembles the former.

[3] One case of enteritis in a cow is reported by Borgeaud as due to them. Cf. *Bakt.*, vol. xxxix, Ref.

gangrene, as well as in cerumen from the ear and in the nasal secretion. Attempts to associate various acid-proof bacilli in the same class with the true parasitic forms of tubercle bacilli, on the ground that guinea-pigs inoculated with them react to tuberculin similarly (Zupnich), or that extracts made from cultures known as "paratuberculin" resemble tuberculin (Irimescu), and that they can immunize against tuberculosis to a certain degree (Klemperer, Moeller, Friedmann), are open to the objection that many non-specific bacterial substances can produce like results. Nevertheless, these experiments and those of Koch, who showed that specific tuberculosis-agglutinating serum caused agglutination of grass bacilli and precipitation of their culture fluid, suggest group reactions comparable to those of the typhoid and colon bacilli, and, therefore, relationship.

**Differentiation.**—*Differentiation by Staining.*—All forms of tubercle bacilli stain deeply with acid-fuchsin-phenol or aniline-water, but retain the stain with varying tenacity under treatment with acids and alcohol. In general, the pseudobacilli decolorize more easily than the true parasites. According to Abbott and Gildersleeve they can generally be decolorized by 30 per cent. nitric acid. The smegma bacillus usually loses the dye upon repeated treatment with alcohol, but in doubtful cases such tests are unreliable, and inoculation should be done.

*By Culture.*—The differences in reaction produced in broth cultures are noted elsewhere. Theobald Smith and Bang consider that the human can be differentiated from the bovine and avian types in this way.

*By Biochemical Reactions.*—Bonome claims that specific differences in precipitating power can be determined by means of the serum and plasma extracted from tubercles, which serve to distinguish bovine from human infection.

**Biology.**—The tubercle bacillus is a facultative parasite, requiring conditions for its growth outside of animals which do not exist in nature so far as known.[1] The requirements are: (*a*) temperature between 29° C. and 42° C. (optimum 37.5° to 39° C.), (*b*) moisture, (*c*) a moderate amount of oxygen, (*d*) protection from light, and (*e*) suitable pabulum containing easily assimilable nitrogen and phosphorus. Its multiplication is relatively slow, being far outstripped by most bacteria, and this fact alone would render its existence difficult except in pure culture, since the associated organisms would soon exhaust the soil. The tubercle bacillus is non-motile and grows more rapidly and more luxuriantly the less is its virulence; coincidently it becomes less sensitive to change of culture media. These observations coupled with its well-known loss of virulence after prolonged cultivation have suggested the possibility that at a remote period in the past it may have possessed a saprophytic existence in nature, a property long since departed from it in its struggle to adapt itself to animals who had received it with their food.

The property of pleomorphism has led some bacteriologists to regard it as an abortive form of a fungus, unable to complete its cycle of development as a parasite. The discovery in recent years of a series of saprophytic, acid-resisting bacilli which resemble the tubercle bacilli and under certain

[1] The possibility of a limited reproduction in the moist sputum deposited in a warm, moist, and dark room may not be denied. Some unconfirmed experiments by Arthur Ransome would point to its sanitary importance.

conditions can produce tubercles in animals (in the sense of nodular cell collections) strengthens the idea that they all belong to a common group the individuals of which have been modified by different environment and selectivity. They are also alleged to have interacting, immunizing, and agglutinating powers and allied chemical products. Notwithstanding these properties, the constancy of the four different parasitic types and their readiness to return to parasitic conditions, whereupon their virulence is quickly restored, prevent such generalizations about the tubercle bacillus at present.

**Transformations into Other Types and Variations in Virulence.**—Conclusive proof is thus far wanting of an actual or permanent transformation of one type into another by passage through animals or by culture. Much interest was excited in this subject by Koch's announcement of the non-identity of human and bovine tuberculosis in 1901, and it was still a subject of difference of opinion at the Paris Congress of 1905. On the whole, the evidence is against such a change, although an increase of virulence of the supposedly human type for goats and cattle is apparently shown by the inoculations of v. Behring, Pearson and Ravenel, and especially by Dammann and Mussemeier and Karlinski. Against these are the negative results of Theobald Smith, Kossel, Weber, and Heuss. Others represent the opinion that transition forms exist between the two types (v. Behring, Dorset, Fibiger and Jensen, Eber, Rabinowitsch, L. and M.). Practical difficulties stand in the way of an easy solution of the question, and also the determinations of inherent differences of virulence grade of the human type for man by inoculation into rabbits and guinea-pigs. That these differences exist is apparent in the varying clinical course of tuberculosis in certain families where the source of infection may be assumed to be the same for each member. Some are mild and chronic, others acute and rapidly progressive; nor can assumed differences in susceptibility always account for this.

From the extensive work of C. Fränkel on the question of differences in virulence, there would seem to be considerable variation between cultures from human sources in this respect. Furthermore, the capacity of some tubercle bacilli for homogeneous growth in liquid media is accompanied by a marked loss of virulence and points to a reversion to saprophytic existence, since many pseudotubercle bacilli possess or assume this property. Variations in the chemical composition of tubercle bacilli and the products of their growth in cultures are also associated with difference in virulence.

**Cultivation.**—Difficulties beset the cultivation of the mammalian bacillus from the tissues of the diseased animal, and it grows reluctantly at first on most media. The first evidence of growth to the eye is a group of minute dull or glistening points after five to ten days, rarely less than eight days. The increase is slow, but in three weeks the surface is covered either by a thin, dull pellicle or small, mealy grains, isolated or crowding together, which form slowly heaping-up masses or wrinkles. During active growth mammalian bacilli preserve a dull, ground-glass, grayish-white appearance which, when multiplication is suspended, slowly become moist and soft if water or glycerin is still present. In drying and in the presence of oxygen old cultures of the human type become reddish brown and even reddish colored on certain media, especially potato; the bovine type does not show this property. The multiplication of tubercle bacilli is presumably by end fission, which results in peculiar S-shaped curls or tapering, curved tufts in beginning growths; these are composed of masses of parallel rods and are

caused by the longitudinal crowding of the young bacilli. In stained preparations of undisturbed colonies the curls are well shown and the individual bacilli are seen cohered by an amorphous, cement-like substance. In old dry cultures which retain the stain poorly, except at the brilliantly stained nodes or "spores," the appearance of the parallel bacilli has been aptly compared to a school of infant fish swimming in one direction.

Freshly isolated cultures from animal tissues on serum or egg tubes are usually shorter, more homogeneously stained, and uniform in size than further transfers on other media. Under some conditions of rapid growth the youngest bacilli, being poor in protoplasmic wax, may retain the stain but faintly under acids: "*primitif bacilles*" (Marmorek). The tubercle bacillus will not grow directly from the animal tissue in a liquid medium, but the thin pellicles which spread over the condensation water of serum cultures, or scales carefully lifted from the solid surface, are transferred easily, floated upon broth, and grow luxuriously as a wrinkled crust over its surface. The broth underneath remains clear, which fact provides a rough test for the absence of contamination. Should the flakes become agitated and the crust wet, the growth ceases and the soaked bacilli sink to the bottom. Owing to its need for oxygen the tubercle bacilli grow readily on the surface of broth, but by special manipulation some cultures may be trained to grow homogeneously through the liquid (Arloing and Courmont). Frequent shaking is necessary to accomplish this and the avian type is best suited for the purpose. The power of motility is claimed for such bacilli, but it cannot be regarded as anything but "Brownian" or "molecular" motion.

*Isolating Pure Cultures.*—Koch succeeded first in isolating pure cultures by the use of coagulated blood serum, and it remains to-day one of the best sources of fresh cultures. Dorset's egg medium is probably the simplest and easiest method for isolating pure cultures from tissues. It is made by breaking fresh, cleansed eggs into a sterile flask and thoroughly mixing the yolk and white, after which the mass is strained through sterile cheese-cloth and distributed into sterile tubes. No neutralization is required and the tubes may be coagulated at once at a temperature of 78° C. inclined in a blood-serum oven, or, better, heated three successive days at 70° C. Before use, a little sterile normal salt solution or water is best added to the bottom of each tube to preserve moisture.

After scorching the surface of a fresh tuberculous spleen, lung, or other organ with a hot scalpel or spatula, bits of the subjacent cheesy or otherwise tuberculous tissue are torn out and squeezed between the broad blades of forceps or sterile glass slides, from which they are quickly transferred by a platinum loop or spatula to the surface of the egg and gently rubbed about on the middle of the slant. Tearing the surface of the medium is to be avoided, and to be favorable the surface should be fragile and elastic.

*From Sputum.*—This may be done very successfully by means of Hesse's agar[1] if a fresh sputum rich in bacilli is at hand. The contaminating bacteria

[1] The formula is:

| | |
|---|---|
| Heyden's Nährstoff[2] | 5 gm. |
| NaCl | 5 " |
| Glycerin | 30 " |
| Agar | 10 " |
| Sol. $Na_2Co_3$ (cryst.) 28.6 per cent. | 5 cc. |
| Water | 1000 cc. |

[2] Other albumose foods, such as somatose or nutrose, are said to be equally good.

in sputum do not thrive on this agar; so the tubercle bacillus has a chance to grow. The method is as follows: A bit of morning sputum is selected and examined for bacilli. If abundant the bit is transferred from one dish of sterile normal salt solution to another, through five to ten changes, shaking it in each dish. After draining the surplus moisture from the particle of sputum, on the side of the last dish, it is gently dragged in a circular direction over the surface of a Petri dish containing Hesse's agar, thereby leaving a delicate trail of sputum. Incubation for four days in a moist chamber is sufficient in many cases to show minute curls or tufts, which may be seen under a low power, and can be identified as uncontaminated bacilli and transferred by a platinum wire to serum, egg, or agar in pure culture. This procedure avoids a long delay in obtaining them by animal inoculation.

*By Inoculation.*—For this guinea-pigs are best and should receive the sputum under the skin of the abdomen. The animal should be killed in three or four weeks—not permitted to die, since terminal infections are likely to defeat attempts to cultivate the tubercle bacillus by contaminating the tubes.

*Culture Media.*—A great variety of culture media are available for the tubercle bacillus. As stated, blood serum is most useful in isolating fresh, virulent cultures; it is best prepared in Loeffler's mixture, but not coagulated as hard as for diphtheria cultures. Dog, sheep, and beef serum are to be preferred in the order named; as already noted, eggs are the best substitute. Sputum agar has been employed successfully. Potato slices to which 2.5 per cent. glycerin-water has been added and calves' brain serum (Ficker) are also useful for isolating cultures from animal tissue. For further growth 3 to 5 per cent. glycerin agar is useful. All kinds of broths and vegetables besides synthetic media are very successfully used. Cultures for diagnostic tuberculin are now usually made on beef broth with 2.5 per cent. glycerin.

*Synthetic Media.*—Various peptone-free media and inorganic salt solutions, introduced by Kühne, de Schweinitz, and Proskauer and Beck, have been valuable in the chemical investigations of the bacillus. It was found that a thrifty growth took place even upon ammonium carbonate, potassium phosphate, magnesium sulphate, glycerin, and water. The notable peculiarity about culture media for the tubercle bacillus is the high degree of acidity due to acid salts which is favorable for their growth.

*Duration of Life.*—Tubercle bacilli in cultures retain vitality at least six months if preserved from drying. They may die in three weeks when not so protected, or at least cannot easily be revived by transplantation. Avian cultures retain life much longer, according to Maffucci, who recovered cultures and produced infection after two years. A more important question is the vitality of the human bacillus in the (clinically healed) diseased foci where the bacilli are encysted and dormant. The observations on this subject are unsatisfactory. Cornet infers that their life is short in the tissues because of the difficulty in growing cultures from old tubercles. On the other hand is the fact of apparent latency for years, during which time all evidence of growth has ceased, yet recurrence of the disease may ultimately occur in the immediate vicinity of the former focus; this is especially manifest in lupus. The early inoculation experiments by Baumgarten with "latent" tubercles and those of Kurlow and Lubarsch with healed tubercles indicated

the persistence of virulence in old caseous tubercles not yet calcified or only partly calcareous.

Schroeder and Cotton's results from inoculations of virulent human bacilli into calves, which produced localized subcutaneous abscesses, are significant of considerable latency. Guinea-pigs were readily infected from the pus after periods of five months to one and a half years. Positive results from inoculations have been obtained from lymphoid tissue where no signs of tubercles were discovered (Loomis, Weichselbaum and Bartel, Rosenberger). How long these bacilli were actually latent or had suspended growth is, of course, uncertain, but experiments by Weichselbaum and Bartel, Perez, and Manfredi and Frisco on rabbits tend to show that their vitality is limited to but few months, when the inoculations remain latent without further growth. The general result of inoculation experiments indicates three to six months as the period during which the bacillus may live in the tissues *without multiplying*, although clinical observations are difficult to harmonize with this statement. Weakening of virulence has been noted by Manfredi and Frisco in their experiments, but Harbitz was unable to detect any differences in this respect in lymph glands from children of different ages.

**Presence of Tubercle Bacilli Outside the Body.**—The human sputum being the chief source of the tubercle bacillus, it is naturally present in the dust of infected rooms, besides being attached to the furnishings, walls, and floors of such rooms. It is rarely found in the open except in the dust of crowded streets, and the enormous dilution of the air and water renders it very infrequent in nature. The customary disposition of urine and fæces render these sources of small account. The presence of bovine bacilli is practically limited to the stables of cattle and hogs with open or ulcerated tuberculosis, and these are uncommon. The exhaled breath is free from bacilli, but they may escape in all other excretions and be secreted in milk. Altogether, the opportunities for tubercle bacilli outside the body are directly dependent upon the degree of cleanliness used in the disposition of the sputum, urine, and fæces, and their presence in milk from tuberculous cows. Cornet made it clear in his investigations that the presence of bacilli was only to be assumed in places frequented by careless consumptives.

**Powers of Resistance.**—*Heat.*—The lowest fatal temperature for the tubercle bacillus is 55° C. (131° F.) moist heat, acting for a period of six hours (Cornet). Dry heat is borne to 100° C. for an hour without killing the bacillus, according to Schill and Fischer in experiments with dried sputum. Moist sputum may be sterilized in five minutes by boiling in water, but thick masses require a longer time. The thermal death point for tubercle bacilli in milk is of great practical importance, and many experiments have been made which determined that from 60° C. (140° F.) to 75° C. (167° F.) was sufficient if continued for one hour. More recently, Theobald Smith, Hesse, Bang, and others have shown that the usual method of pasteurizing milk at about 60° C. to 65° C. in an open vessel or bottle is insufficient to kill them, since they come to the top in the scum and thus remain cooler than the underlying liquid. Therefore, if pasteurization is desired the milk should be stirred or placed in a closed vessel and heated at least twenty minutes to 65° C. (149° F.). Bang concluded that 85° C., the Danish legal requirement, was a sufficient temperature to sterilize the dairy refuse fed to calves and hogs.

*Cold.*—The tubercle bacillus is not destroyed by any degree of cold. The experiments of Galtier, by which alternate freezing and thawing of tuberculous tissue was tried for several weeks, showed no decrease in virulence; those of Cadeac and Malet preserved vitality four months. Cornet found frozen dry sputum virulent after six weeks; Twichell with frozen moist sputum found the same after nearly four months. Swithinbank found liquid air ineffective on cultures, but alternations of thawing and freezing were destructive to virulence.

*Drying.*—Dry bacilli from cultures may lose virulence in three weeks, but the more important question as to their vitality in naturally dried sputum involves such varying conditions that the preservation of infective power depends upon the size and thickness of the sputum mass, its quality, its place of deposit with reference to the character of the surface, and, most important of all, its exposure to light, heat, and air. When sputum of tenacious character is dried in large masses the bacilli are shut out from the air in the hard, glue-like crusts; and in a dark, cool place, such as a basement room or the corridor of many city dwellings, the maximum period of vitality may be assumed to be from six to eight months; this is the estimated limit given by Cornet as the result of his own and numerous other researches. A valuable series of studies by Flügge and his associates in recent years have revised to some extent the conclusions of Cornet as to the virulence of dry sputum in dust which is capable of floating in the air. The ingenious experiments of Kirstein with sprayed and dried sputum brought into the form of dust, indicate but a short lifetime for bacilli thus exposed to air and in diffused daylight. The following were his conclusions: Dust from library books was found infectious after eight but not after fourteen days; powdered sputum alone, after four but not after seven days; lint from sputum-smeared clothing, after five but not after ten days; sputum mixed with street dust, after three but not after eight days.

*Water.*—Experiments by Chantemesse and Widal showed that the bacillus tuberculosis could live in sterilized water from the Seine from fifty to seventy days. Galtier preserved them four months in water. The influence of light and decomposition hasten their death under natural conditions in water.

*Putrefaction.*—Putrefaction of sputum and tuberculous animal tissues usually destroys the tubercle bacillus within a few days (Baumgarten and Falk, de Toma, Schill and Fischer). It is dependent, however, on the nature of the process and how rapidly it takes place whether the products of decomposition are harmful to the bacillus or not. Galtier was able to infect animals after two months with putrid spleen and lung. This question is of interest in relation to the persistence of virulence in the diseased cadavers and excreta of man and animals because of the possible danger of transmission by means of infected earth, insects, etc. Cadeac and Mallet found buried tuberculous lungs virulent after five months, but Klein not after seven weeks. Gärtner concluded that tubercle bacilli could survive months in fæces. Lortet and Despeignes showed that earth-worms could harbor bacilli when in contact with sputum, but decomposition ordinarily must obviate danger from such sources.

*Symbiosis with Other Bacteria.*—In the experiments by Prudden on mixed infection with *Streptococcus pyogenes* the tubercle bacillus was not prevented from growing on broth by their presence. Bonhoff found that they were

restrained when thus grown together, but the explanation may be simply that the reaction was altered or the nutrient material lessened.

*Gastric Juice.*—The tubercle bacillus can be destroyed by the normal gastric juice in a test-tube experiment, but this result is due to the hydrochloric acid and not to the pepsin. Under actual conditions in the living stomach there is little likelihood that all the bacilli are killed because of the varying acid strength and their mixture with food. The experiments of Falk, Straus and Wurtz, Cadeac and Bournay, Zagari, and Ferranini agree in the conclusions that bacilli introduced into the stomach with food, sojourn too short a time to be killed.

*Light and Other Radiations.*—The effect of light is distinctly injurious to the tubercle bacillus. Koch's first observations indicated that cultures were sterilized in a few minutes' exposure to strong sunlight when in thin layers. Diffused daylight required from five to seven days. Here, again, the natural conditions under which tuberculous material may be exposed to light play a very important part in determining the degree of its disinfectant power. The experimental observations give very wide ranges as to the time required to kill tubercle bacilli in sputum exposed to the sun under varying conditions. For example, Migneco, in Italy, found sputum virulent after ten to fifteen hours' sunning, but not after twenty to twenty-four hours during the hottest hours. Mitchell and Crouch, in Denver, Col., found that sputum deposited in sand remained virulent from ten to thirty hours. Delepine and Ransom used a variety of tests with dried sputum and in the form of dust, which showed a loss of vitality after one to eighteen hours' exposure. Jousset and also Twichell exposed sputum from one to seven hours and found it occasionally innocuous. These results taken together show that a speedy death of sputum bacilli occurs when it is exposed in a dry and dusty condition to sunlight or even diffused daylight. Experiments by Bang, in the Finsen Light Institute, with unconcentrated electric (arc) light acting on cultures, usually killed the bacilli in from three to nine minutes' exposure; nevertheless, the probability of some direct bactericidal influence upon lupus bacilli in the tissues is very slight, since Klingmüller and Halberstaeder excised bits of tissue, after a period of seventy minutes' treatment, which were infectious for guinea-pigs. The Röntgen rays have been found to be bactericidal to some extent for the cultures of the tubercle bacillus by Rieder, who excluded light and heat rays in his experiments. De Renzi, however, did not discover any effect on sputum. Radium has probably a harmful effect on tubercle bacilli as on other bacteria (Pfeiffer and Friedberger), but no studies are recorded on the former.

*Antiseptics, etc.*—The tubercle bacillus is more resistant to chemical disinfectants than most pathogenic bacteria, except anthrax and a few other spore-bearing forms. It is, however, restrained from growth in cultures very readily even by volatile agents, such as hydrofluoric acid (Villemin and Trudeau), formaldehyde, creosote, oil of eucalyptus, peppermint, etc. The commonly used disinfectants, phenol, mercuric chloride, and formalin require a long time to disinfect moist sputum by reason of its ability to resist penetration on account of the coagulation produced on the outer surface which protects the inner portion. Five per cent. phenol is slow in action, requiring twenty-four hours in Schill and Fischer's tests upon sputum, while even 2 per cent. mercuric chloride was not effective. Since the practical usefulness of disinfectants must depend upon the penetrative power,

those which have a solvent action are to be preferred. In this class is lysol, which is effective in 1 per cent. solution. Other combinations of soap and the kresols are very valuable. Two per cent. lysol is the most useful agent to disinfect sputum in cuspidors, but its odor is prominent; caustic alkalies and strongly alkaline soaps suffice in suitable receptacles to render sputum harmless. Calcium hypochlorite is an excellent disinfectant for sputum and fæces. The use of formaldehyde gas has practically displaced sulphur for the fumigation of rooms, and the results are satisfactory in disinfecting the surface of objects exposed for a sufficient time to the moist vapor in a well-sealed room; this is, unfortunately, not always accomplished, and bedding, rugs, and other objects likely to have folds, if contaminated with smears of sputum, escape disinfection. Masses of sputum large enough to be visible cannot be rendered harmless by ordinary fumigation. The numerous iodine preparations used in surgical tuberculosis and employed internally have only a weak germicidal effect directly upon the tubercle bacillus, but slowly liberate iodine in the tissues and possibly exert a restraint upon the growth in this way.

**Chemical Composition of the Tubercle Bacillus.**—The facility with which large quantities of tubercle bacilli can be grown on fluid culture media made chemical analyses far more feasible than with most bacteria, and the use of proteid-free solutions of chemically pure salts for media has still further aided in exact determination of the products of growth. De Schweinitz and Levene have made a special study of the latter. Hammerschlag was the first to publish an analysis of tubercle bacilli, he having found a peculiar acid-resisting proteid substance in broth and agar cultures. The most important analyses have been made by de Schweinitz and Dorset, Proskauer, Ruppel, and Levene.

**Elementary Analyses.**—The composition of tubercle bacilli varies considerably with the medium upon which they grow, as shown by the following from Levene:

| | | Broth per cent. | Mannite (synthetic) per cent. |
|---|---|---|---|
| Alcohol and ether extracts = | Fat | 31.56 | 22.18 |
| | C | 55.58 | 47.41 |
| | H | 8.46 | 7.05 |
| | N | 9.39 | 7.91 |
| | S | 1.39 | 0.25 |
| | P | 0.59 | 2.67 |
| | Ash | 5.92 | 10.00 |

More than one-half of the ash consisted of phosphorous pentoxide, with sodium, calcium, and magnesium oxides in about equal quantities for the remainder. De Schweinitz made determinations of the phosphorus contained in the ash from virulent and weak-virulent human cultures, which indicated a less phosphorous content for the virulent and also for the bovine bacilli, corresponding with their lesser fat-content.

**Nucleoproteids or Nuclein.**—Mucin-like substances were originally extracted from the bacilli by Weyl and Hoffman and identified by Kühne and de Schweinitz as nucleoproteids. Later, Ruppel and Levene independently examined the reactions and analyzed the decomposition products of this important ingredient, which proved to contain the essential poison. This is a peculiar nucleic acid present in the body of the bacillus and its

soluble secretions. Water dissolves one-half of the pulverized bodysubtance and the solution is precipitated by acetic acid, but contains no ordinary coagulable proteid. The cement-like substance which agglutinates the bacilli in masses is composed of this nucleoproteid. Digestion of the bacilli with pepsin or trypsin removes but little substance, and saline extracts also contain very little simple proteid. Levene discovered three forms of nucleoproteid in bacilli grown on synthetic media and extracted by 8 per cent. ammonium chloride; they differed in solubility, heat coagulation point, and phosphorous content. The so-called toxins formed in the broth cultures are identical with these and appear to be dissolved out of the bacilli rather than secreted from them.

**Nucleic Acid or Tuberculinic Acid.**—The decomposition of the nucleoproteid above described sets free a special nucleic acid containing from 9 to 11 per cent. of phosphorus. It can be precipitated by alcohol and forms the most toxic substance yet isolated from the tubercle bacillus. By further decomposition tuberculinic acid is split into thymin and a neutral substance called "tuberculosin" (Ruppel), besides several bases. Levene and Kitajima also found thymin in the nucleic acid. The effects of tuberculin are ascribed by v. Behring to the thymin fraction in the nucleic acid. In the precipitated nucleoproteid is found "tuberculosamin" (Ruppel), a protamin which is a base in combination with the nucleic acid. The most striking peculiarity of this toxic nuclein is its extraordinary resistance to heat and chemical decomposition. It has also unquestionably important disease-producing capacity and constitutes in all probability the essential endotoxin of tubercle bacilli.

**Fats and Wax.**—Second only in importance to the nuclein are the fats of the tubercle bacillus. De Schweinitz and Dorset, Aronson, Kresling, Bullock and McLeod, and Ritchie have made exhaustive analyses of these, with the result that a great variety of extracts have been isolated. Estimates of the proportion of fat in the bacilli vary from 10 to 40 per cent., far in excess of all other bacteria; and the quantity depends on the age, rapidity of growth, virulence, and composition of culture medium. Bovine and virulent human bacilli were found by de Schweinitz and Dorset to have less wax than weak-virulent cultures. The fatty acids isolated have been partly identified as palmitic, lauric, butyric, oleic, etc. Cholesterin, lecithin, and other alcohols have been found. The alcohol and acid resistance is ascribed to an, as yet unidentified, alcohol by Bullock and McLeod. Von Behring holds that the true vaccinating substance of the intact tubercle bacillus is a combination between a lecithin and a nuclein.

**Other Components.**—Cellulose has been detected by some chemists and carbohydrates of the sugar class by others. Bendix found a pentose and Levene discovered glycogen in combination with the nucleic acid.

**Secretions during Growth.**—There is no evidence that tubercle bacilli secrete or excrete anything in cultures during active growth except a trace of volatile fatty acid and a slight amount of soluble nucleoproteid having the same reactions and properties as that obtained by maceration or extraction of the bacilli. It is probably set free from degenerated or dead bacilli. The fatty acid is the source of the almond-like odor developed in cultures. Alkaloids and toxalbumins have been described by various investigators in the past, but improved chemical methods have failed to demonstrate them. They corresponded in their reactions to the heat-coagulable nucleoproteids

found by Levene in the culture filtrates. Differences between the acidity of human and bovine broth-culture filtrates have been noted by Theobald Smith, which he regards as a means of identification. The human broth cultures have an increased acidity, while the bovine become more alkaline. The significance of this has not been determined definitely, although the higher percentage of free fatty acids found by de Schweinitz and Dorset in human bacilli is suggestive, since the presence of glycerin was found to bear some relation to the production of the acid reaction. Bang has confirmed Smith's observations and also found that the avian bacilli behave like the bovine in producing an increased alkaline reaction.

**Tuberculin.**—This term was applied at first by Koch to the filtered and concentrated broth in which full-grown cultures had been boiled. It contained, therefore, a glycerin-broth extract of the bacilli, together with such soluble products of the bacilli as were formed during their growth and not precipitated or destroyed by heat. This original tuberculin, or "T. O." (also called "old tuberculin," "A. T."), was the first of several modifications experimented with by Koch.

Analyses were made of crude tuberculin by Proskauer and Brieger, and especially by Kühne, who found an albuminate and a peculiar "acro-albumose," not present in the broth constituents, but present in cultures on proteid-free media. Further analyses by Ruppel identified the active substances in tuberculin with the nuclein and tuberculinic acid previously described. It is precipitated by 66 per cent. alcohol and the re-solution of this precipitate was called "purified tuberculin." Tuberculin in this form when subjected to tryptic digestion wholly loses its activity, thus indicating its essential combination with proteid. It is, however, very resistant to physical and chemical agencies, heat, light, etc., and loses but little activity in concentrated form by age.

*Modifications.*—The various modifications of tuberculin merit description with reference to their nature and mode of preparation, although the use of some has been abandoned. Hunter's and Trudeau's modifications were attempts to precipitate the active substances with ammonium sulphate and by dialysis to purify the residue from salts.

Tuberculocidin and Antiphthisin (Klebs) represented the precipitate obtained in a similar way after the removal of the so-called alkaloids by potassium-bismuth-iodide.

Oxytuberculin (Hirschfelder) was the original tuberculin treated by boiling in hydrogen peroxide ($H_2O_2$).

Tuberculoplasmin (Hahn) was the fluid expressed from fresh bacilli by hydraulic pressure.

Tuberculol (Landmann) contained extracts of tubercle bacilli prepared at different temperatures separately, then combined and evaporated at a low temperature.

Water extract (Maragliano) consists of the concentrated extract of tubercle bacilli digested for six days on a water-bath at 90° to 95° C. and filtered.

Water extract (v. Ruck) differs from the last mentioned in that the washed bacilli are first extracted with alcohol and ether, pulverized, and then extracted with water at 50° C.

Tuberculin (Denys) ("B. F.") is the unaltered filtrate from broth cultures.

"Perlsucht" tuberculin (Spengler) is made from bovine bacilli, after the manner of the original tuberculin.

Tuberculin (Beraneck) is prepared by evaporating *in vacuo* the full-grown culture filtrate to one-tenth the original volume, the broth containing no peptones in its composition. The concentrated filtrate is then precipitated with 60 per cent. alcohol and the residue collected. The bacilli are extracted with 1 per cent. orthophosphoric acid at 70° C., and the two products mixed in equal quantities.

Various tuberculins were also prepared by Koch, Weyl, Vesely, Arloing and Guinard, v. Behring, Thamm, and others, representing alkaline or other extracts of tubercle bacilli, and which were used chiefly in animal experiments.

Paratuberculin is the name given to extracts of pseudotubercle bacilli prepared like the original tuberculin.

*Tuberculosis Vaccines.*—Tuberculin R ("T. R.") (Koch) was introduced in 1897 as an improved form of tuberculin for immunizing as well as therapeutic use. In contrast to the various extracts it is an emulsion of the residue from living, virulent bacilli after pulverization and extraction with water.

"Bacillen emulsion" ("B. E."), Koch's latest product, consists of an emulsion of the entire substance of the pulverized living bacilli in 20 per cent. glycerin, only the coarser particles being excluded. Glycerin is depended upon to sterilize any bacilli not removed by centrifugalization.

"Bovovaccine" (v. Behring) is the first immunizing virus introduced by v. Behring for cattle, and consists of unsterilized dried bacilli from a human culture passed through guinea-pigs. It is used intravenously and keeps but one month.

"Tauraman" (Koch and Schutz) is the analogous vaccine for cattle introduced by Koch, but is preserved in a more virulent condition. It is used intravenously.

"Tuberculase" or "T. C." emulsion = "Tubercle Cytin" (v. Behring), is the latest immunizing agent whose nature and method of preparation, so far as has been made known, consists of an emulsion of the bacillus residue after extraction successively with alcohol, water, 10 per cent. sodium chloride, and other extractives as yet undescribed. The bacilli, which are further treated with chloral hydrate and are still intact, are said to be unable to grow, yet are easily absorbed by the tissues without producing tubercles. They nevertheless create tuberculin susceptibility for a time. Its use is restricted to animals.

"Tulase" (v. Behring) is described as related to tuberculase, but is a clear, yellowish, honey-like liquid for therapeutic use on animals and human subjects, and contains all the constituents of tubercle bacilli, including the latter in a condition for easy absorption.

"Tulaselactin" is the latest name applied by v. Behring to his tulase prepared in the form of a milky emulsion, and which is said to possess but slight tuberculin-reacting power when fresh, but owing to instability acquires it after a short time. It then becomes weak in immunizing power.

It may be said of the various tuberculins that, viewed from a chemical standpoint, they all contain the peculiar nuclein substance or its derivatives in greater or less quantity and degree of solubility. In some the endotoxin has been altered or decomposed by heat or extractives, but all are capable

of producing the characteristic reaction in tuberculous subjects.[1] The vaccines form either preparations of living bacilli or their substance as nearly unchanged as possible.

**Chemical Pathology.**—*Action of Dead Bacilli.*—It was early demonstrated that dead bacilli could produce tubercles essentially identical with those caused by living bacilli. Caseation is, however, absent unless large amounts are injected, which generally leads to abscess formation in subcutaneous injections. Besides the local effects, Maffucci and his pupils showed that nephritis, atrophy, and disturbance of nutrition such as are seen in the cachexia of advanced tuberculosis can be produced by sterilized bacilli. Recent investigations by Cantacuzene on the changes in fatal poisoning by dead bacilli freed from wax, show that an acute necrosis of the cardiac muscle, renal epithelium, and polynuclear leukocytes takes place and that eosinophiles appear in abundance in the blood. Von Behring also regards the leukocytes and lymphatic tissue as having a special affinity for the specific toxin, and describes cell metamorphoses recognizable by staining, due to the bacillus residue or "tuberculase."

Koch, in the experiments upon tuberculous guinea-pigs which led to the discovery of tuberculin, found that dead bacilli injections modified the course of the disease so as to cause healing of the inoculation ulcer; many others confirmed and extended these observations.

*Effect of the Nuclein.*—As already mentioned, nearly all the extracts obtained from tubercle bacilli contain the poisonous nuclein or its decomposition products. The effect of moderate doses on healthy animals of the water or glycerin extracts is not immediately harmful. Repeated large doses produce fever and wasting without noticeable microscopic changes. Large doses cause death in healthy guinea-pigs in twelve to forty-eight hours from slow collapse, the only microscopic lesions being local extravasations at the site of injection. In tuberculous animals very small doses cause high temperature and local reactions at the seat of disease, accompanied by a polynuclear leukocytosis. Very moderate doses cause death in a few hours, with hypothermia, leukopenia, and extensive extravasations of blood about the tubercles. Von Behring and Ruppel prepared pure tuberculinic acid whose toxicity was very great for tuberculous guinea-pigs, but further decomposition of this toxin weakened its effect. De Giaxa also produced coagulation necrosis with the nucleic acid prepared from tubercle bacilli. In its most insoluble form the nuclein or endotoxin which remains after thorough extraction of the bacillus is the most prolonged in its poisonous effects, and probably gives rise to the so-called "tuberculin hypersusceptibility,"[2] because of its very slow absorption and the specific adaptation required of the cells to absorb and disintegrate it.

*Effect of the Wax.*—When isolated in a pure form, the alcohol, ether, chloroform, or benzole extract has the effect upon the tissues of an insoluble irritant. Auclair has produced caseation by means of the ether, chloroform and xylol extracts, and ascribes to the fatty secretions of the bacilli the case-

[1] It is claimed by C. Spengler and Bandelier that bovine tuberculin (Perlsucht T. O.) is less active on human subjects than the human, while Kanda found the opposite for cattle. Quantitative differences are not readily excluded in such tests.

[2] Von Behring now believes this results from an affinity between the so-called cytin cell-substance and a similar substance ("T. C.") in the tubercle bacillus.

ating property of the tubercle bacillus. It is undoubtedly true that the fatty acids in tubercle bacilli play some part in the coagulation necrosis of tubercle, but it is very doubtful that they are the chief agents.

Volatile distilled products of tubercle bacilli have not been isolated in quantities sufficient to establish their probable importance in the disease. The local effects of tubercle bacilli may fairly be attributed to the highly resistant wax, combined with the necrotising action of the nucleic acid and fatty acids. It is uncertain whether these caseating substances are chiefly set free during the multiplication of the bacilli or after their death and disintegration. The soluble products of the bacilli which have thus perished are unquestionably the cause of the constitutional symptoms in tuberculosis, such as the fever and anæmia. Moreover, the toxæmia closely resembles that produced experimentally by the nuclein or dead bacilli above described. Maragliano claims to have found a toxin in the blood and urine of cachectic consumptives which produced tuberculin effects, while others have demonstrated albumoses in the urine (Lenoir) and sputum (Simon) which resembled tuberculin.

The question of a selective action of the toxin for certain tissues has received attention by v. Behring in recent years, and his researches led him to the opinion that the leukocytes and endothelia of the alveolar capillaries and serous membrane are the especially sensitive cells. On the basis of this theory he explains the local reaction to tuberculin.[1]

*Effect of Tuberculin.*—The phenomena of tuberculin poisoning have already been described as those of the endotoxin or nuclein of the tubercle bacillus. The chief interest centres about the local reaction in tuberculous foci and in the acquisition of tolerance or immunity to this poison by all the tissues. In moderate doses no perceptible effect is produced upon the tissues or blood in health. Large, repeated injections into the veins have caused endarteritis, degeneration of liver and kidney epithelium, followed by atrophy of these viscera. All forms of tuberculin act similarly in causing local reactions about tubercles, but vary greatly in the time and intensity of the reaction, owing to their greater or less solubility. The original tuberculin acts more violently than some of the modifications, doubtless because it contains more of the simple derivatives split off by heat from the macerated bacilli.[2]

[1] *"Aggressive" Activity.*—The parasitic power of the tubercle bacillus is ascribed by Bail to a special "aggressin," a secretion or body substance by which the leukocytes are repelled or injured, thus permitting the bacilli to grow. According to this theory, the ability of various bacteria—tuberculosis, anthrax typhoid, etc.—to grow in animals is due to this aggressive property. Experimental evidence of such a substance so far has been unsatisfactory in the case of tuberculosis, for products of the bacilli obtained from the animal or extracts in the test tube from dead or living cultures, whether of high or low virulence, accelerate death in healthy guinea-pigs without preventing phagocytosis, as found by Baldwin and Price. Von Behring states that water extracts of highly virulent bacilli are more toxic than those of weak virulence and that the virulent bacilli are less readily phagocyted. It is not clear, however, that a toxin or "aggressin" of different nature accounts for these differences. The hypothesis of Theobald Smith, who suggests that the bacillus becomes surrounded by a protecting envelope as it becomes more parasitic, has more plausibility than that of an "aggressin."

[2] It furthermore contains the constituents of the broth-culture medium, peptone and beef extractives, unused by the bacilli in growth. These have some enhancing influence upon the reaction in large doses, but for the purposes of diagnosis, for which it is principally used, this is inappreciable.

*Local Reaction.*—The marked local selective action upon the tubercles which characterizes tuberculin requires detailed description, for it illustrates the mechanism by which the tissues combat the disease.

Following the administration of tuberculin, within four to twelve hours, dilatation of the small arterioles and capillaries surrounding the tubercles takes place, and a serous and cellular exudate follows sufficient to cause visible swelling in the case of lupus; the zone of lymphoid and epithelioid cells already about the foci becomes augmented by additional cells, chiefly polynuclear leukocytes, and in violent reactions extravasations of red cells may appear. These phenomena reach their height in from six to twenty-four hours and quickly subside, unless very large or quickly repeated doses are given. After forty-eight hours lupus foci have become smaller and less conspicuous than before; and when favorably treated the lymphoid cells are either gradually absorbed or transformed into fibrous tissue as in the natural cicatrization of tubercles undergoing healing. The local reaction varies in intensity according to the situation, extent, and age of the tubercles, as well as in the sensitiveness of the cells composing the tubercles in responding to the toxin.

Neither the local nor general reaction is absolutely specific; various nucleoproteids, yeast nuclein, bacterial proteids in general, and digestive products, such as albumoses, are capable of producing similar effects. Cinnamic acid, cantharidin, pilocarpine, and other alkaloids also act to some degree, although less as local irritants than general leukocyte stimulants. There are analogies in other diseases with focal points of infection, such as anthrax, syphilis, and streptococcal infections, where local and general reactions may result from a specific stimulus. Moreover, tuberculous subjects are well known to be markedly sensitive to fever from transient mental or physical excitement as well as digestive disturbances. It is unnecessary to suppose that there is an actual local reaction in all such cases, although it can be observed at times in lupus and laryngeal ulcerations. A slight increase in the lymph flow from the heightened blood pressure can cause more absorption from the foci. These facts have tended to discredit the value of tuberculin as a delicate diagnostic agent, but in practice need not cause confusion in cases of recent tuberculosis.

*Theories of the Reaction.*—The explanation of the reactive phenomena has been puzzling, and several contradictory theories have been proposed which need not be reviewed. The most satisfactory theory, which accords with the modern immunity studies, is in essence that first proposed by Eber, Babes and Proca, and modified by Theobald Smith, which assumes an enzyme activity in the cells immediately surrounding the bacilli and their products. Under ordinary conditions a slow disintegration and digestion of the bacilli take place, but with the added stimulus of tuberculin injections the process is accelerated in the foci; if enough irritation has occurred, soluble or partly digested products of the bacilli are freed which are sufficient to cause local and general reactions. It is also possible that in severe local reactions precipitation or coagulation of the toxin occurs in the small arteries or capillaries nearest the tubercles, as v. Behring held in his explanation of the reaction. It is not to be assumed that this alone or invariably is the cause of the congestion, but the antibodies are presumably set free to a greater extent by the cells most under the influence of the toxin. Whether the function of these cells be twofold—*i. e.*, precipitating and fermentative or

not, both phenomena appear to play some part in the reaction. Recently v. Behring reasons that the thymin substance in tuberculin has an especial affinity for the "T. C." or cytin of the tubercle bacillus which has previously combined with the body cells and is the cause of their sensitiveness. It is, hence, capable of removing it from its combination and thus creating the reaction. It is not clear that an enzyme function is excluded by such an explanation.

Repetition of the injections in increasing doses gradually creates a tolerance which is explained in two ways: (*a*) By the neutralization of the tuberculin by antibodies before it reaches the tubercle (probably precipitins), and (*b*) the exhaustion of toxin accessible to the reacting cells. The tolerance is consequently not a lasting one, as the reaction power may return after cessation of the injections so long as cells remain which retain sensitiveness.[1]

**The Mechanism of Resistance and Immunity.**—The animal tissues present a certain degree of normal resistance against the invasion of the tubercle bacillus and poisoning by its toxins. It is obvious that the normal resistance may become gradually increased by many exposures which have been successfully overcome without the development of actual disease; this general biological law finds no exception in the case of tuberculosis, although in case the infection has once taken root in an individual, even if recovery takes place, a subsequent increased susceptibility appears to follow in many instances, as in scrofula.

The protecting mechanism is feeble in infancy, but if early infection is avoided or successfully prevented without a foothold gained by the bacilli, the adult human individual in normal health seems to be practically immune to natural infection. From the present aspect of the problem of infection, we must conclude that the mucous membranes and lymphatic tissues are chiefly concerned in the primary resistance to tubercle bacilli rather than the pulmonary alveoli, as formerly supposed. These facts are of the utmost importance, and are deduced from many observations in the past which harmonize with experimental evidence in recent years on animals, and have been further strengthened by the studies on latent tuberculosis of Harbitz, Rosenberger, Furth, and others.

According to the present view, in primary infection the bacilli are able to reach the lymph nodes connected with their path of entrance without necessarily leaving any trace at the latter, and create no apparent response to their presence for some time. If, however, they survive the normal lytic action of the cells, they may be carried farther or excite the local reactive process, which leads to tubercle formation. The struggle for mastery is essentially a local one, although, as in miliary tuberculosis, many foci may begin simultaneously. Lymphocytes are prominent in the formation of the tubercle, and the wandering leukocytes participate together with connective-tissue cells in localizing the bacilli. If the organism is successful in effectually localizing the invaders, a more or less rapid process of disintegration or bacteriolysis ensues which destroys the bacillus and disposes of its products, possibly leaving behind changed cells in the tissues as a consequence of

[1] Wasserman and Bruck found both antituberculin and tuberculin in the tubercles and gave an explanation of the reaction on the theory of local antibody action; their method was only conclusive in showing the presence of tuberculin, as shown by Weil.

their absorption of some specific ingredient of the bacillus which stamps tuberculin susceptibility of longer or shorter duration on the individual. On the other hand, many cells may die in consequence of the direct and prolonged exposure to the toxin and caseation of greater or less degree is the common result, which really protects the enclosed bacilli from further lytic action by the living cells. The tubercle forms, therefore, the object of study as the unit or type of the mechanism of resistance; for the tissues in general experience but slight effect from the presence of a few tubercle bacilli well localized, and there results a lack of effective resistance from absence of a general stimulus at favorable moments in most cases of chronic tuberculosis. The ultimate result consequently often depends on the efficiency of the cell nutrition throughout the body to bear repeated severe exposures without harm.

**Heightened Susceptibility to Reinfection and Tuberculin.**—This characteristic is one of the results of a previous infection and may arise from partially healed or latent tubercles as well as recent active disease. Koch first noted that a second infection produced marked reaction at the point of inoculation without spread of the infection from this point, and it led to his discovery of tuberculin. Von Baumgarten also studied the phenomena of primary and secondary infection. Straus and Gamaleia observed that great sensitiveness had been acquired by animals injected with dead bacilli to a repetition of the injections.

The analogous results with tuberculin are well known, severe and even fatal reactions being possible in tuberculous subjects from doses which are practically inert for healthy persons. The subject has been thoroughly studied by v. Behring, Theobald Smith, Trudeau, and others, and the conclusion is unquestionable that the phenomenon is one of specific resistance. There are analogous hypersensitive reactions resulting from the injection of various foreign serums and other proteids, the so-called "serum disease," whose symptoms and period of development are closely comparable and leave no doubt of a close relationship. Von Behring finds in *natural* infection of calves that three months is the usual period required for tuberculin susceptibility to develop to a noticeable degree. It requires from eight to fourteen days after experimental inoculation in guinea-pigs. From this time fever and local reactions follow the injection of tuberculin or allied proteids. This period is the same which is required for the formation of all kinds of antibodies, and we may infer that the development of reaction susceptibility signifies a lytic power or an affinity acquired by the cells of the tubercle acting both on its own accumulated toxin and the injected tuberculin, which liberates a poisonous substance or combination affecting the whole organism.[1] This susceptibility has an important bearing both on the development of new foci in the presence of existing disease and the acquirement of immunity of which it is probably a phase.

So long as this susceptibility persists, there is reason to expect that new infections with tubercle bacilli will be localized at the point of entrance into the tissues, and that they are either disposed of there without actual infection

[1] The delicacy with which the reaction occurs in response to minute doses of tuberculin in the incipient stages of tuberculosis is often increased by repetition of the same dose within short intervals. This fact forms the basis of a method of tuberculin diagnosis advocated by Loewenstein and Rappoport.

or produce foci with ulceration, as in the larynx and intestine during the later stages of pulmonary tuberculosis or during periods of lowered resistance.

The reaction power implies a certain change in the organism in reference to the tubercle bacillus toxin which causes an immediate response by the tissues; this is obviously intended to fix and destroy the bacillus, and is the result of specific antagonistic powers developed or latent in the body from an existing or previous infection. The reason why this condition does not mean efficient immunity in all cases is explained by Theobald Smith as due to the greater vulnerability of the lungs where a second infection is prone to occur and be focused, instead of being carried into the lymph nodes and destroyed as in a primary infection. An external exposed focus in a more vulnerable tissue is thus to be regarded as more dangerous for the individual whose specific immunity is incomplete than for one in whom only normal reacting power exists. Such may not, however, hold good for an exposure to bacilli outside the body where the number of bacilli is infinitely less than from ulcerating tubercles in the diseased person. Von Behring, from his extensive investigations in cattle tuberculosis, regards this sensitiveness in the light of an actual acquired predisposition, and believes that it can persist for some time in cattle after an inoculation of human bacilli, even where no tubercles can be found. He is inclined, nevertheless, to doubt that this predisposition favors a renewed infection from without; rather does it oppose this, but promotes its further spread in the individual with *already latent* disease. In the present state of our knowledge this reaction susceptibility cannot be considered a necessarily unfavorable factor in an adult individual who has a clinically healed pulmonary tuberculosis. Its duration after this stage in man is unknown, but it remains at least for ten years.[1] It was not transmissible to the calves born of immunized cows in the Marburg experiments, yet Cornet admits the possibility of an inherited toxin susceptibility, although assigning small importance to it as a predisposition.[2]

**Immunity.**—No disease has shown so little evidence of apparent immunity conferred by one attack as tuberculosis; the contrary is the universal clinical experience on superficial observation. Nevertheless, there are certain characteristics of the clinical course of the disease, and in some cases of recovery, which on closer examination point to an acquired resistance which amounts to practical immunity. Even the more chronic course of the disease, seen, as a rule, in persons classed formerly as "hereditarily disposed" and scrofulous, but now regarded as instances of early infection, may be regarded as a sign of specific resistance.

Likewise, the slow progress and often benign course of tuberculosis in subjects beyond middle age are readily attributable to an acquired resistance due to previous infections.[3] Both Turban and Solly found a greater percentage of chronic, prolonged, arrested cases among those patients with family tuberculosis who do not die in the onset of the disease than those without such a history. Unfortunately, such comparatively mild infections

[1] Personal observations of the author.

[2] Rosenau also offers the suggestion that tuberculin susceptibility may be transmitted to offspring, as he has shown to be possible with serum anaphylaxis, and thus form a predisposition to tuberculosis.

[3] The exacerbations during the course of the disease often have a well-defined limit, ranging from ten to fifteen days, which is significant when taken in connection with the period of antibody formation in the blood after bacterial inoculations.

as are seen in persons with weak constitutions of phthisical build are not really often recovered from in the sense of restoration to robust health; the disease no longer progresses, but secondary anæmia, weak digestive function, and poor assimilation frequently accompany an actual disappearance of the former symptoms. There is in consequence but slight reason to speak of an advantageous immunity conferred by previously healed tuberculosis in such persons: too often it plainly produces the opposite effect, or is only a transient heightening of resistance. H. M. King has made the interesting observation that the course of the disease in 103 fatal cases was a year longer in subjects of phthisical parentage than in those without it. Such facts speak quite as much for acquired resistance from repeated early infections as for inherited immunity. Nevertheless, the acquisition of relative immunity by certain families and races which have long been subjected to the conditions of life favorable to tuberculosis and exposed to the infection, has considerable support in connection with the Jewish and English races, who have intermarried less with other races than those of Central Europe. Reibmayr holds this theory and predicts a diminution and decreasing virulence of tuberculosis comparable to that of syphilis.

**Experiments in Tuberculosis Immunity.**—The first encouraging results from experimental researches on tuberculosis immunity and specific treatment began with Koch in Germany, Hericourt and Richet in France, and Trudeau in America in 1889-90. A host of others have followed with notable contributions, among whom de Schweinitz, MacFadyean, Maragliano, Pearson and Gilliland, Koch, and Neufeld should receive special mention. Von Behring and his associates have unquestionably made the most extensive investigations, and practical results are already apparent in his "bovo-vaccine" method of immunizing cattle with human bacilli, and the coincident application of the same principle by the American veterinarian, Pearson.

The very persistent studies and animal experiments in this field have at least demonstrated that a high degree of artifical protection is possible against tuberculosis. Complete immunity under extreme conditions of experimental inoculation has proved disappointing as compared with some other diseases. Nevertheless, it is reasonable to state that the problem has been practically solved so far as the bovine race is concerned, although the duration of the protection is yet uncertain and may require years to determine. It is not too much to hope that harmless immunization of very young calves may be accomplished to such a degree that natural infection will be powerless against them when supplemented later by the natural resistance of adult life, even if the specific resistance then fails. It is even possible that a safe immunization may be applied to human infants, as v. Behring, Valleé, and others hope from their recent experimental work. It is premature to conjecture how long such protection would last, but if sufficient to prevent infection during childhood it would be conceivably of great value. The prospects for a passive or transferred immunity by means of serum, milk, or otherwise are less promising.

The production of immunity by means of serum or by extracts of the bacillus has thus far failed, and preparations of the living bacillus have provided the best protective vaccine for animal experiments. Some increase of resistance can be obtained by the injection of the various tuberculins and dead bacilli, and it is to be hoped that still better results may be possible along this line without the necessity for the use of living organisms. An

ideal vaccine should theoretically contain all the immunizing properties of the living bacteria in a form both incapable of infection and easily absorbed by the tissues; these qualities are claimed to be possessed by v. Behring's "tuberculase" and "tulase."

**The Mechanism of Specific Immunity.**—Specific immunity against tuberculosis, in the meaning at present understood of immunity to bacterial diseases in general, requires an ability on the part of the tissues to disintegrate the bacillus and destroy or neutralize its toxin; in short, a combined bacteriolytic and antitoxic immunity. Whether this form of expression correctly states the problem as applied to tuberculosis or not, there are facts that point to a bacteriolytic function which may be evolved by various methods of immunization. The question as to the production of a literal antitoxic property is yet a matter of conjecture, for when bacteriolytic power is developed to a high degree, there may still be a lack of complete tolerance of the toxin. It is, hence, possible that the disease may be arrested for a time, only to result in a chronic poisoning because of the bacilli disposed of in greater numbers, and whose toxin the tissues have inadequate power to neutralize at the time most needed. There follows in consequence permanent injury to the cells.

Many clinical facts attest the truth of the above statement and explain the succession of arrests and relapses in the course of the disease. Possibly because of the unequal rise and fall of the two necessary functions complete immunity is made more difficult.

Owing to the restricted action of the toxin, the cells not composing the tubercle fail to get the proper stimulus to resist its action when the constitutional condition is in a favorable state for this. It is also fairly established that such immunity as is acquired by an animal to this disease rests in its cells and is not discoverable in the behavior of its serum. This fact forms the chief *rationale* for specific therapy in tuberculosis by tuberculins, for it is desirable to impress the whole organism with the specific stimulus in sufficient quantities and at proper intervals to maintain a high resistance. The exact mechanism of the acquisition of increased tolerance by the cells is undoubtedly a very subtle thing and closely connected with the tuberculin susceptibility phenomena. Elaborate and abstruse hypotheses are offered by v. Behring. Briefly stated, they assume a physicochemical process of union between a lecithin-proteid substance contained in the tubercle bacillus and certain constituents of cytoplasm which have an affinity for it. A transformation follows that eventually adapts the cell for future attacks of the toxin. The duration of specific immunity is as yet unknown.

It is assumed by v. Behring that the lymphatic tissues and leukocytes are especially concerned in maintaining immunity. However this may be, the excessive inflammatory reaction seen in experimental inoculation of immunized animals is accompanied by a large collection of mononuclear and polynuclear leukocytes about the bacilli and all the phenomena of a prolonged tuberculin reaction. Since complete absorption of the focus and disappearance of the bacilli may follow without caseation resulting, it is natural to suppose that the process is an immunity reaction, even though it be only an exaggeration of the normal one which results in caseous tubercles in the unvaccinated animals. In calves immunized by v. Behring, tuberculin-reaction susceptibility must wane before he regards them as sufficiently protected, but this would mean a perfect tolerance on the part of the cells,

with an unfavorable condition for the growth of the bacilli whose mechanism is not as yet explained.

**Antibodies.**—Agglutinins or precipitins are readily produced against tubercle bacilli and their products by repeated injections of these substances, and appear to some extent in the course of the disease, as found by Arloing and Courmont. A high agglutination power nevertheless may exist without immunity, as in the course of typhoid fever. A close relationship obtains between the precipitins and agglutinins of tubercle bacilli as they are interacting upon the solutions and emulsions of the bacillus substance.

*Opsonins* which aid in the phagocytosis of tubercle bacilli have been distinguished as specific antibodies quite distinct from the agglutinins by Wright and Bullock, and have some similarity to the serum complement. This function prepares the bacilli for ingestion by the leukocytes and can be increased by tuberculin injections. It may therefore have some bearing on the production of immunity, but its relative importance is yet undetermined. Neither can the opsonic index alone nor the agglutination test at present be regarded as a measure of immunity nor of absolute diagnostic value for tuberculosis, because normal agglutinins and opsonins which act on tubercle bacilli to a greater or less degree are present in healthy persons.

*Antitoxins or Antituberculins* have been demonstrated by Maragliano and others in the serum of animals injected with extracts of bacilli. Their true nature is in doubt, and although they have been shown to neutralize fatal doses of tuberculosis toxin, it is not clearly established that they are analogous in action to those of diphtheria and tetanus, whose toxins are of a different nature. It is difficult to disassociate the possible action of a lysin and precipitin, both of which are probably present in these serums as in those from animals injected with other bacterial proteids and bacteria (typhoid, cholera, etc.). The presence of a bacteriolysin has indeed been claimed for Maragliano's serum.

*Bacteriolysin.*—It has been difficult to experimentally demonstrate a bacteriolytic power in serums acting on tubercle bacilli *in vitro*, probably owing to the inherently great resistance of this organism to disintegration and the long time required for such action. Moreover, the participation of living cells may be an essential condition not susceptible of imitation in the test tube. The existence of such a function is nevertheless undoubted, as progressive stages of disintegration in the bacilli which are introduced into immunized animals are manifest by staining.

The therapeutic experiments with antituberculosis serums have usually been disappointing or unconvincing as to a specific value. Some have proved harmful, like those of Maffucci, Bâbes, and v. Behring. Furthermore, too little attention has been given to the physiological effect of repeated injections of heterologous serums apart from any specific antibodies that they may contain.[1] Whether the specific precipitins, opsonins, or antitoxins found in the serum are essential to a high resistance is at present only conjectural; they at least accompany the development of specific resistance or active immunity in animals, but attempts to transfer the immunity to others by means of the serum have not succeeded. Therefore, the outlook for a successful serum therapy in tuberculosis cannot be regarded as hopeful at present.

[1] Normal serums alone under these conditions have been shown to excite antibodies against the serum *per se*, whose effects must be reckoned with.

To summarize the present knowledge of specific reaction products against tuberculosis, we can say that specific agglutinins and opsonins are readily recognizable in the serum and that probably lysins and toxin-assimilating or digesting functions exist which act in conjunction with the body cells to produce relative immunity.

**Conditions Influencing Infection.**—It is hardly possible to enumerate all the factors involved in bringing about infection in tuberculosis, since they must be regarded as extremely complex in many instances and far wider ranges obtain between susceptibility and practical immunity than in the other infectious diseases. It cannot be said, as in cholera or diphtheria, that, given an equal exposure, a large percentage of individuals will develop the disease in a virulent form. Moreover, there is a strong probability that the slowness of reproduction which is characteristic of the tubercle bacillus furnishes a better opportunity for the animal host to create an adequate defence, whereas there is no time for this in the more acute diseases. In any consideration of these varying conditions leading to infection both parasite and host are subjects of possibly equal importance in determining the balance of power.

**Number and Virulence of Tubercle Bacilli.**—On the part of the tubercle bacillus the dose and virulence must be conceived to be of prime importance. It has been shown in animal experiments that a moderate infection may be completely overcome while a greater one is fatal. It is thus intelligible that repeated and frequent exposures seem ordinarily necessary to produce the disease in human adults. If a single exposure were sufficient, the fact would be difficult to prove anyway, because of the slow development of the disease; yet its occurrence cannot be considered impossible, especially in children. The actual number of bacilli in room-dust capable of floating in the air is small compared with those in the heavier particles of moist or dry sputum on the floor or contaminated clothing which cannot remain suspended. Hence, the number of bacilli swallowed must be much greater than those inhaled, however they are taken in, and a single exposure might be sufficient to infect a child in this way.

The virulence is also known to be variable. Some strains of tubercle bacilli are able to infect in the minutest dose when implanted in susceptible animals, while others seem very feeble. Clinically this fact may be only surmised by the different forms of the disease, whether chronic or acute, and by instances of apparently direct contagion, where the disease develops in rapid succession in a number of unrelated individuals. On the other hand, the most virulent strains of bacilli are weakened by drying and exposure to light and air, which conditions usually exist to some extent in indirect infection and which probably neutralize or delay the manifestation of differences in virulence. What the virulence of a given strain may be is difficult to determine from the course of the disease in human subjects, where so many other factors enter into the problem.

**Natural Resistance of the Human Organism.**—In analyzing the nature and mechanism of man's natural resistance to tuberculosis, one must include his environment relative to climate and altitude; his residence, whether urban or country, together with his occupation and cellular defences. An invigorating climate inviting to an open-air life is an obvious advantage, while elevation above sea level promotes increased function and strength of the heart and lungs. The greater purity of the air and less strenuous

life of the country dweller naturally contribute to the maintenance of normal vigor.

In the first rank for the natural protection of the individual is the epithelial covering of all surfaces exposed to external influences. The external skin is not easily penetrated by tubercle bacilli unless a lesion exists, and it offers an effective barrier in adult life, though less in childhood. The nasal and pharyngeal mucosa with intact ciliated epithelium is a strong defence, as is also that of the trachea and bronchi; the normal adult gastro-intestinal tract likewise appears but slightly permeable. If the infection gains entrance, there are other mechanisms set in operation which tend to fix the bacilli at the portal of entry or to check its progress in the neighboring lymph nodes. These are comprehended under the head of immunity reactions, elsewhere considered. An intimate knowledge of their nature defies our present powers of research, but some insight has been obtained.

The determination of the opsonic index appears to be one measure of resistance which we possess to-day, although its limitations are not yet fully known. When the complex nutritive processes are better known, other reactions of equal value may be discovered. At present the sum of our knowledge of good physiological resistance is expressed indefinitely as good cell nutrition. Hence, good eaters with sound digestions are well armed against this disease. The gouty diathesis is undoubtedly an evidence of relatively greater resistance to tuberculosis according to clinical experience, while certain diseases mechanically oppose it. Mitral heart disease with resulting pulmonary venous stasis acts as a protection possibly for that reason, yet the matter is rather too complicated for positive proof. Emphysema is also supposed to afford some degree of immunity against tuberculosis. An open-air occupation or one requiring active muscular exercise is another important aid to resistance. Musicians who play wind instruments are infrequently tuberculous, according to Rogers.[1] Certain occupations have been claimed to be especially protective against tuberculosis because of the gases inhaled by the workmen. Such are the sulphurous acid fumes produced in the so-called sulphite process in the manufacture of wood-pulp, also those of ordinary coal-gas and ammonia. The proof of such a protection is not convincing enough for serious attention. Agricultural pursuits and a seafaring life are naturally best adapted to maintain a strong constitution if other conditions are favorable. Lastly, a naturally vigorous mental and moral equipment is second only to the physical.

**Reduction of Resistance.—Disposition.**—A well-founded belief in a "tendency" to tuberculosis has existed in all ages of medical history. It received a check at the time of the discovery of the bacillus, and is still belittled by the contagionists (Cornet). A broader view has again taken root which modern biological research supports, and which claims the acceptance of a middle ground, giving due prominence to both the parasite and host in disease production.

*The Nature of Disposition.*—A satisfactory definition of the actual nature of what we term disposition or predisposition is as yet wanting. In the last analysis it has to do with the cell activities of the animal body. It may include a positive element in that the soil is abnormally favorable by reason of a certain chemical composition or functional excess of the tissue metabolism,

[1] *Medical Record*, October 6, 1906.

or, on the other hand, a negative one which consists in the absence of some chemical ingredient or weakness of the normal defensive mechanisms. On the surface, the chemical theory of predisposition has support in the well-known susceptibility of diabetics, because sugar is known to be a favorable component of culture media for the tubercle bacillus. The grade of alkalescence of the blood and especially of the bronchial mucus has also been suggested as a factor (Hesse), since an alkaline sputum is a more favorable culture medium. There are other theories, such as variations in the composition and structure of the elastic fibers (Hesse, Tendeloo); in the amount of silicates in the connective tissue (Kobert, Schulz); the "demineralization theory" of the French authors (Robin and Binet), which assumes a deficiency in the tissues of mineral salts, especially of calcium and the phosphates, due to increased respiratory change or excess of oxidation and the converse of the gouty or arthritic diathesis, which is accompanied by an excess of these salts. All these theories have found support in the analyses and experiments of their authors, but are too narrow and lack completeness for a subject of such complexity.[1] The studies in hæmatology and antibodies of the serum have led to the probability that a subnormal resistance is associated with a deficiency in certain forms of leukocytes (Arneth) and of normal alexins and agglutinins in the blood fluids. More recently the valuable work of Wright and his associates indicates that a lowered opsonic index or deficient phagocytic power is a sign of predisposition which promises much importance.

A subnormal resistance to tuberculosis may be: (1) From causes arising within the body—(*a*) natural and (*b*) acquired. Under natural causes we shall consider (1) Race; (2) Heredity; (3) Individual constitution; (4) Age; (5) Sex.

**Natural Predisposition.**—*Race.*—The question of racial differences in susceptibility has already been noted. It is yet undecided what factor or factors are most important in the apparently greater vulnerability of the Negro and aboriginal Indian races. An attractive theory is that they at present lack the gradual immunity acquired by more resistant races through centuries of civilization and exposure to the infection, the more resistant individuals having survived among the latter. From this point of view racial susceptibility is simply a passive quality rather than a peculiarly different soil.

*Heredity.*—One of the most complex problems in medicine is that of an inherited disposition to tuberculosis. Theories have changed as new facts have developed, but the belief in such family inheritance is well-nigh universal. Elaborate statistical studies and genealogical tables have been made by Riffel, Leudet, and others to show the predominant influence of heredity, even to the one-sided view that the infection is of secondary importance; on the other hand, Cornet, v. Behring, and Boeg ascribe little if any importance to heredity. Practically the only question to be decided is whether an inherited weak constitution has a *specific* tendency to implantation of the bacillus. Little value can be placed upon genealogical data to settle this question, for the impossibility of excluding congenital or infantile infection is apparent. Testimony for and against specific inheritance from family records is of equal importance. For example, Riffel gives the history of

[1] A good review of the subject is found in the very complete work of Schlueter, *Die Anlage der Tuberculose*, 1905.

several generations of tuberculous families where the infection could fairly be excluded in some descendants who became tuberculous. However, Cornet criticises this study for gross inaccuracies. On the other hand, Boeg studied the mortality from tuberculosis among the Faroe Islanders, who are closely intermarried and have had no opportunities for outside infection, but he found no support for the inheritance theory. J. E. Squire gives more valuable evidence against the importance of specific susceptibility by comparing the children of consumptive parents with those of non-consumptives of the same class and condition in life. He found only 10 per cent. more of the former had become tuberculous in a study of 1000 families, an excess easily accounted for by the greater opportunities for infection rather than actual heredity.

A truly specific inherited susceptibility must imply transmitted properties through the germinal cells, and strictly construed should not include influences acting during intra-uterine life, which are really congenital. Adami believes that two possibilities may result from parental tuberculosis: according as the disease is progressive or unresisted the germinal cells become weakened by the specific poison and the offspring especially susceptible to tuberculous infection; or if well resisted the child may acquire an increased resistance to the same disease. Some experimental support to this idea has been attempted, but the matter is difficult to control.[1] Moreover, the argument of Hueppe, who is an exponent of the importance of disease predisposition, may be adduced, that "immunity and immunization directly prove biologically that predisposition must be a positive property of the protoplasm, for otherwise there could be no immunization."[2]

In a matter of such subtlety, future studies may make the truth clearer, but certain clinical observations tend to confirm a belief in an inherited specific susceptibility of a certain kind. One of the most interesting and suggestive is that of Turban on the inheritance of a *locus minoris resistentiæ*, whereby the disease was found to begin in the corresponding lung of the parents and the children in 19 families out of 22 (86.4 per cent.). Among the writer's cases 78 per cent. of 28 families where parental tuberculosis existed had children with the corresponding lung first involved. In one family the father and four children had the same lung first affected. Ogilvie found similar instances. A striking example also of the apparent transmission of susceptibility is found on the Isle of Man, where tuberculosis is nearly twice as frequent as in England and Wales. Davies, who made a study of the conditions there, concluded that consanguineous marriages for many centuries were chiefly responsible for the excessive amount of tuberculosis.

The youngest child in large families was found by Brehmer to be more

[1] Carrière claimed that the young of animals injected with toxins of tubercle bacilli were more easily infected than those of control animals. Sicolla and Palmieri found the progeny of tuberculous guinea-pigs abnormally susceptible to tuberculin. Analogous hypersensitiveness to certain poisons appears to be transmissible from parent to offspring.

[2] The transmission of tuberculin susceptibility to the calves from immunized cows did not occur in v. Behring's experiments, nor is it reasonable to expect the influence of tuberculosis toxins to be manifest in the offspring unless the disease is active in the mother during pregnancy; it is entirely problematical how paternal tuberculosis can have any influence.

susceptible than the older children, but Shively in a critical study of 1175 cases in families of four to thirteen children came to the opposite conclusion.

The inheritance of nutritional faults and structural defects in the chest, size of heart and arteries, the so-called "paratuberculoses" (Hutinel, Mosny, Landouzy), etc., which are elsewhere mentioned as important disposing factors, cannot strictly be classed as specific qualities established by the parental disease in all cases, since they may proceed quite certainly from non-tuberculous individuals. Nevertheless, for practical purposes, these observations cannot be ignored because the matter is complicated and not necessarily connected with tuberculosis in the parent.

Defects of development or diseases in the parents often stamp sufficient weakness upon the offspring to constitute a lessened resistance to tuberculosis quite as important as that entailed by tuberculous parents upon theirs. Prominent among these parental diseases is syphilis; alcoholism and various psychoses are also regarded by many as of great importance. Statistics which will bear criticism have not been taken as to the relative incidence of tuberculosis among the children of such parentage, but as less than a third of tuberculous individuals give a history of tuberculous parentage, it may be assumed that other diseases and abnormalities in the parents have no small part in whatever hereditary weakness may be attributed to the remainder. It is, therefore, only in the broadest meaning that the inheritance of predisposition to tuberculosis can be considered of especial importance, *i. e.*, any defects or injurious influences acting upon the parent may possibly be a source of predisposition for the child.

*Constitution or Habitus Phthisicus.*—Constitutional weakness or maldevelopment (whether truly inherited or congenital) has always claimed importance as a disposition to tuberculosis. Hippocrates described the *habitus phthisicus* as the blonde, delicate-skinned individual with winged scapulæ and long, flat chest. Besides the delicate, ovoid-featured type of persons with long, thin bones, known as the tuberculous by the older writers, the scrofulous was also recognized, with broad face, thick lips and nose, coarser skin, and heavier figure. These two types have been fairly distinguished in composite portraits made in recent years by Galton and Mahomed of 442 tuberculosis patients, thus confirming the accuracy of the early observations. In olden times no account seems to have been taken of the numerous exceptions among consumptives who were without structural defects, nor could a distinction be made during the "prebacillus era" between the inborn and acquired changes resulting from the disease itself. In consequence of greater enlightenment these constitutional factors have lost some of their import, although many of the so-called stigmata of tuberculosis undoubtedly favor the disease. Rokitansky was one of the first to give a detailed description of the *habitus phthisicus*, and laid stress on the poor muscular development and shape of the chest—a narrow anteroposterior diameter, but of greater length than normal, and with small abdomen. The lung volume, however, was considered proportionately greater. By the careful clinical studies of Brehmer and the pathological ones of Beneke still further anomalies became recognized. According to Brehmer, voluminous lungs were associated with an abnormally small heart, which therefore failed to adequately nourish them, thus predisposing to the disease. His system of sanatorium treatment, especially the gradual hill-climbing, was based on this theory, and was supported by 500 anamneses and thousands

of observations. Beneke found in many comparative measurements, besides large lungs and small hearts, relatively narrow arteries and short intestines.

Bony deformities of the nose and jaws which cause mouth-breathing are now properly included among the constitutional defects. The life insurance companies of today doubtless wisely retain the old conceptions of predisposition in their inquiries about the shape and expansion of the chest and the relation of height to weight, although the tall individual with immobile, flat chest, depressed sternum, and sloping shoulders can no longer be considered necessarily a bad risk. The recent measurements of Brown and Pope of the patients at the Adirondack Cottage Sanitarium tend to deny any special type for the tuberculous chest, although there was some tendency for the thoraces to be slightly rounder, flatter, and of greater length than normal. The favorable types of the disease, however, are selected for this institution. Among 647 patients of a poorer class in the clinic at Cracow, Poland, only 38 per cent. exhibited a phthisical form of chest, 41.6 per cent. with and 36 per cent. without tuberculous heredity (Kwiatkowski). Turban, whose patients belong to well-to-do classes, found 36.3 per cent. with an *habitus phthisicus*. It is evident that many anomalies when combined in the same person may form a constitutional disposition, but singly have little importance, since they may be compensated for without impairment of the general vigor.

**Local Predisposition.**—A local disposition natural to certain tissues or organs, especially the lung apices, has much interest and possible importance. Most of the theories urged as the cause of primary apical disease can be expressed by the term local malnutrition. The mechanical theory of the older authors, which attributed the local weakness to a lessened aëration and greater opportunity for the retention of dust due to the poorer expulsive power of the apices, has become less tenable since the knowledge that by hæmatogenous infection as well the apices are primarily involved in man. Nevertheless, the observations of Birch-Hirschfeld that a small posterior apical bronchus is an especially favorable situation for primary bronchial tuberculosis includes not only a mechanical theory but also that of local malnutrition. This author has shown that these bronchi are deflected at a sharp angle from the larger tubes, and because of the slower air currents the opportunities for gathering foreign matter are much greater than in the lower lobes, where the respiratory movements are stronger. The stagnation of secretions and poorer aëration are also a source of lowered resistance to the tissues, whether the infection be aërogenous or hæmatogenous. An abnormally great predilection for this situation in some individuals, according to Birch-Hirschfeld, is caused by congenital or acquired irregularities, with narrowing of the posterior apical bronchi. The possible relation of Turban's inherited *locus minoris resistentiæ* to this fact is noteworthy.

Freund first called attention fifty years ago to a narrowing of the apices associated with a premature ossification of the first rib cartilage which restricts the development and causes greater immobility of the apex. Hart,[1] in an exhaustive monograph, has recently emphasized anew the importance of Freund's theory in local predisposition and the inheritance of this anomaly. He considers that it gives rise to a shortening of the first rib and a "stenosis"

[1] *Die Mechanische Disposition d. Lungenspitzen*, etc., Stuttgart, 1906.

of the apex, and is dependent upon deficient development of the first-rib cartilage or the rib itself on one or both sides. Rothschild,[1] furthermore, found the same predisposition connected with insufficient movement at the sternal joint between the corpus and manubrium at Louis' angle, which is favorable to the paralytic type of thorax. Schmorl discovered a furrow on the lung surface extending diagonally downward from the posterior aspect of the apices, where the pleura was thickened and near which the primary tubercles are formed. Cornet thinks the greater frequency of right apical diseases is due to the larger right bronchus receiving more dust.

Taken separately these various anatomical theories do not carry much weight. When, however, they are combined with the physiological conditions of the blood and lymph circulation in the apices as compared with other regions of the lungs, an explanation of the early involvement of the apices becomes clearer. In the first place the atmospheric pressure variations during respiration are much greater in the basal parts of the thorax, as shown by Meltzer and also by Hofbauer, whereas there are almost no variations at the apices. The consequent lesser aëration and rapidity of the blood and lymph flow in the apices favors the lodgement of the tubercle bacilli, while the same reasons render the tissues more vulnerable. The work of Tendeloo[2] led him to a similar view. It has also been suggested that the upright posture in man favors venous stasis in the lung bases, which in turn forms a hindrance to infection, according to the studies of Bier.

Little can be said in explanation of the apparently greater susceptibility of the lungs, kidneys, and joints as compared with the liver, spleen, and muscular tissues. Aufrecht has long maintained that the presence of terminal arteries in the lungs had much to do with the infection and that the infarcts caused by bacilli in the bloodvessels formed the primary foci. Like conditions may account for localizations in the kidneys and joints. Hence, mechanical and physiological reasons favoring the lodgement of the bacilli sufficiently account for these differences in some cases without invoking a humoral theory or that of a special chemical affinity between certain cell forms and the tubercle bacillus. Future research may associate these latter factors more satisfactorily with lowered resistance than can be done at present.

*Age.*—The resistance to tuberculosis varies with age and is least in childhood, when the tissues readily permit the infection to enter at various places and be more easily distributed. It is also well known that the lymphatic, meningeal, bone, and joint forms of the disease predominate in early life, but after the tenth year the pulmonary form increases in frequency.

Whether this difference is due to a greater susceptibility of these tissues in childhood or to a difference in the avenues and opportunities for infection is a complex problem. As mentioned elsewhere, v. Behring holds that the pulmonary form in adults is chiefly a sequel to gastro-intestinal or other mucous membrane infection in infancy due to the incomplete development and ready permeability of the mucosa, which offers no barrier to absorption. However this may be, there is a tendency in adults for the disease to develop at the site where the infection is presumed to enter in the lungs or mucous

[1] *Der Sternalwinkel* (Angulus Ludovici) in *Anat. physiol. u. path. Hinsicht*, 1900.
[2] *Ursachen der Lungenkrankheiten*, 1901.

surfaces, whereas in childhood it usually spreads farther before the tissues respond by tubercle formation. Evidence is accumulating that a primary infection is far more frequent in childhood than hitherto suspected, and it is fallacious to consider the frequency of tuberculosis at different life periods as an index of susceptibility at those ages. This depends, as Cornet says, upon external causes and varying exposure to infection.

It has been observed that puberty and the menopause in females are epochs during which the disease may develop rapidly. An apparent inheritance of susceptibility at certain ages is observed in some tuberculous families, whereupon the disease begins in the children as they successively reach the fatal age—usually between eighteen and twenty-five. These instances are probably associated with infection at an early age, though the facts are used in support of the theory of actual bacillary inheritance.

*Sex.*—Little difference exists between the sexes in their liability to tuberculosis except that during menstruation, pregnancy, and lactation women are temporarily rendered less resistant. It is even debatable whether pregnancy as such favors susceptibility, but there is no doubt that the strain of labor and the puerperal period give an impetus to the disease if latent and increases the danger of infection. In 46 (5.25 per cent.) of the adult females among the author's private patients, pregnancy, labor, or lactation was the predisposing cause assigned. The female skin being more delicate than that of the male, there is also greater opportunity for local infection. Lupus is nearly twice as frequent in women as in men, according to Cornet's statistics.

**Acquired Predisposition.—Constitutional Diseases.**—*Scrofulosis.*—This much disputed term deserves retention, in the opinion of the writer, only when applied to chronic non-tuberculous enlargements of the lymph nodes, and to the constitutional weaknesses of the skin and lymphatic apparatus well described by Virchow, who regarded the condition as due to a maldevelopment of the glands and lymphatics. Repeated microbic infections other than the tubercle bacillus, such as the streptococcus, staphylococcus, and influenza, can undoubtedly cause a persistent hyperplasia of the lymph glands which give a predisposition for tuberculosis. Whether such instances can be distinguished clinically from actual tuberculous lymphadenitis is indeed doubtful. Opinions are not wanting that the entity known as scrofula always indicates tuberculosis. Cornet differentiates three forms of scrofulosis: (1) Tuberculous, *i. e.*, produced by the tubercle bacillus; (2) the non-tuberculous or pyogenic, chiefly caused by the streptococci and staphylococci; (3) a mixed form in which the first two are associated. He also recognizes a congenital predisposition to scrofulosis, an abnormal permeability of the skin, mucous membranes, and lymph passages which is inherited as well as acquired. Von Behring of late has explained the scrofulous diathesis as due only to the effects of actual tuberculous infection, which alters the lymph and bloodvessels and leaves a tuberculin susceptibility stamped upon the tissues. The arrested infantile tuberculous infection thus prepares the way for a secondary infection and forms a specific predisposition. This aspect of scrofulosis makes the decision no less difficult because the presence or absence of tubercle bacilli, *i. e.*, of an actual latent tuberculosis, is not the criterion, but rather the presence or absence of tuberculin susceptibility. At present the question may still be considered open, while for practical purposes the term scrofulosis can be used to mean an

important predisposition to pulmonary tuberculosis, which is associated with it in 25 per cent. of all cases.

*Diabetes.*—The presence of an excess of sugar in the blood favors bacterial growth and doubtless diabetics are especially prone to tuberculosis for this reason alone, whether or not other factors are of greater moment. It is estimated that one-fourth to one-half of all diabetics, especially young persons, succumb to tuberculosis in a progressive form.

*Syphilis.*—This disease may act as a disposing factor in reducing the general vitality, and both diseases are present in many persons of the depraved class. Turban found a previous history of lues in 6.4 per cent. of 408 cases; Sokolowski in 3 per cent. of 8074 cases; the author, 1.3 per cent. of 1690 private cases. An idea once promulgated that syphilis confers a relative protection against tuberculosis is entirely without foundation.

**Nervous Diseases.**—*Psychoses.*—An irritable nervous system is so frequently associated with pulmonary tuberculosis that neurasthenia, hysteria, or nervous instability in general have long been considered predisposing factors. Papillon even considers neurasthenia as a symptom of suspected latent tuberculosis. The relation of these characteristics to tuberculosis as effects rather than causes is therefore equally probable. It cannot be denied, however, that those persons who possess by inheritance or otherwise a delicate nervous organization frequently fall victims to the disease. T. J. Mays goes so far as to ascribe a nervous origin to all cases of tuberculosis and dependent upon degeneration in the pneumogastric nerve. Here again cause and effect are difficult to separate and too great emphasis is given to a single factor. In the true psychoses there is an undoubted predisposition, especially with imbecile melancholics. Snell found that 41.2 per cent. of the latter died of phthisis and 27.1 per cent. of maniacs. Epileptic families are also prone to tuberculosis.

It should not be thought that the frequent incidence of tuberculosis is the direct result of nervous disorders, but rather that the defective functions and nutrition of such persons render infection easier. Increased opportunity for infection, especially in public institutions, has also played an important part in the past.

**Chlorosis and Anæmia.**—Chlorosis and anæmia secondary to other diseases are to be considered predisposing factors in a limited number of cases. Latent tuberculosis, however, can be excluded in but few of these cases, according to some results obtained by the tuberculin test in late years.

**Previous Disease of the Lungs and Thorax.**—The importance of acute respiratory diseases in developing a latent tuberculosis and favoring a new infection is apparently great. Turban found 34.5 per cent. of his cases preceded by a tendency to inflammations and catarrh of the air passages. The relation of *lobar pneumonia* to tuberculosis is in dispute, some authors holding that the latter is relatively rare as a sequel to pneumonia and that caseous pneumonia begins as such, while others maintain that it is developed from a latent focus by the pneumonic process. Jacob and Pannwitz found 195 in 3295 cases with a history of precedent pneumonia and therefore regard it as predisposing. It was found in 110 of the author's 1690 patients in whom a predisposing cause was assumed.

*Influenza* is a frequent and important agent in bringing to light latent tuberculoses, and during the last decade has become prominent in the histories of tuberculous patients. Allowing amply for mistakes in diagnosis

where the presence of tuberculosis is overlooked, influenza must be classed as an important exciting cause if not a true predisposition. Jacob and Pannwitz found it to have occurred shortly before the tuberculous outbreak in 479 (14.5 per cent.) of their cases; while 389 (11.8 per cent.) gave a history of antecedent colds. Among the author's cases 262 (15.5 per cent.) gave a history of influenza and 376 (22.2 per cent.) of colds.

*Measles, scarlatina, variola, diphtheria, tonsillitis,* and *whooping-cough* are in the same category with the respiratory diseases because the lowered resistance produced by these maladies is accompanied by inflammation of mucous membranes and lymph glands where tubercle bacilli may have already lodged. In order to distinguish between the instances of latent infection which are spread by these diseases and those fresh infections for which the soil is made favorable, the time elapsing before the tuberculous outbreak takes place forms some guide. It may be assumed that the longer the interval the greater the probability there is of a new infection having occurred. Whatever may be the sequence of events, the acute infectious diseases are of the greatest importance in the development of tuberculosis, especially of the lymphatic form in children. Measles and whooping-cough claim the first rank in this connection. In the author's series of 1690 cases, all over 15 years of age, the above diseases preceded the tuberculosis in 61 (3.6 per cent.) cases.

*Bronchitis simplex* and *chronica* in adults have no favoring influence toward tuberculous infection in themselves that can be proved, while *emphysema* is possibly even protective against pulmonary tuberculosis. The frequency of bronchitis and asthmatic affections prior to recognized lung tuberculosis cannot be regarded as causative; rather are they symptomatic of existing tuberculosis. A recent study of 700 cases of *asthma* by Soca indicated that a large proportion (500) were apparently associated with pulmonary tuberculosis. Asthma was given as a precedent disease in 11, bronchitis in 52 of the author's series. Catarrhal diseases of the upper air passages of a chronic character cannot be considered as *directly* aiding infection except in children, considering their frequency in otherwise healthy persons. On the other hand, nasal obstructions and adenoid hypertrophy resulting from catarrhal affections are potent aids to infection by causing "mouth-breathers." E. F. Ingals found nasal diseases in only 28 per cent. of 830 cases of tuberculosis, whereas 75 per cent. of the general population suffer from them. In 29 of the author's cases it was assigned as a factor.

*Pleuritis* of the primary form is in such a large proportion of instances a symptom of tuberculosis that it needs no further mention here. Secondary pleurisies due to trauma, pneumonia, and other respiratory diseases may act predisposingly.

*Rachitis* being an expression of defective nutrition favors infection; presumably both for that reason and because of the thoracic deformities which form a *habitus phthisicus* and impaired chest movements. It was found in 10.8 per cent. of Turban's cases. Well-marked deformity was found in but 41 (3 per cent.) of the author's cases.

*Typhoid fever and gastro-intestinal disease* are undoubtedly occasionally followed by tuberculosis. Opinions differ as to the frequency of tuberculosis following typhoid fever, as the diseases are frequently confused, the diagnosis of typhoid often being made at the onset of tuberculosis. No certain rela-

tionship has been established between the diseases. A history of typhoid fever was given by 74 (4.2 per cent.) of the writer's patients.

*Malaria* is a frequent history obtained from tuberculous patients who reside in malarial regions. Such was given by 49 (2.09 per cent.) of the writer's series. Its actual position as an etiological factor is doubtless much exaggerated by the confusion of the symptoms with those of tuberculosis.

*Genito-urinary disease, nephritis, and carcinoma* are predisposing to some extent, as is also *chronic heart disease* with aortic stenosis. Congenital or acquired stenosis of the pulmonary artery is especially predisposing, whereas mitral stenosis confers an apparent protection against the disease.

**Injuries.**—*Trauma* is important in creating favorable conditions for infection or spreading that which may be present. The ruptured blood-vessels and extravasated blood arrest the bacilli, which may enter the circulation and hence form the nidus for infection after contusions. Joint, pleural, and meningeal tuberculosis is very naturally associated with injuries in the popular belief, and quite justly. Blows on the chest are considered equally important in connection with pulmonary tuberculosis. Five of the author's patients gave a history of blows on the chest and two of falls. Concussions and nervous shocks, such as are produced by falls and railroad accidents, should have place in the etiology of tuberculosis. The relationship of injuries in modern American athletic contests to subsequent tuberculosis may not be unimportant and demands study. Surgical operations upon tuberculous glands and joints are occasionally followed by dissemination of the infection. In 18 of the author's patients, surgical operations (13 being for appendicitis) appeared to play a predisposing part.

**Environment.**—*Causes Acting on the Body from Without.*—Of equal importance to constitutional or acquired weakness are the surroundings and mode of life of the individual. Every relation in life is a factor in some degree for or against the development of tuberculosis.

*Climate.*—The predisposing influence of low, damp climates was greatly overestimated in former times, because of ignorance of the essential infection. At the present day the opinion has reached the opposite extreme, that no importance is directly attributable to this element in man's surroundings so far as tuberculosis is concerned. The truth, doubtless, lies in a mean between these extremes. The debilitating heat of the tropics, with its high humidity and the depressing effect of the fogs and wet winds of the Atlantic coast, must only be contrasted with the invigorating highlands of the interior and the arid deserts and sunny table lands of the far West to admit that climate is a potent factor in physiological resistance to tuberculosis. On the other hand, that it can be a specific predisposition is no longer claimed, for in the statistics adduced to show this, too many uncontrolled factors entered which are of much greater importance. The same may be said of the separate elements of climate, such as altitude, humidity, soil, wind, etc. The classic observations of the late Henry I. Bowditch, of Massachusetts, and of Buchanan, of England, that phthisis prevailed more in districts having wet soil, have lost some of their force with further enlightenment; but it must be acknowledged that the conditions in such places are more favorable for preserving the vitality of the infection, as well as for the development of other diseases which are predisposing, than well-drained regions with dry or sandy soil. Gordon, of England, has also apparently demonstrated, by comparison of countries otherwise similar in race, occupation,

etc., that wet winds increase the mortality of tuberculosis. It is further believed to be more acute in hot climates.[1] On the other hand, no exemption from the disease is found in any climate when the other conditions for infection and development of the disease are present.

*Density of Population.*—The prevalence of tuberculosis is universally greater in cities than in rural communities, and no more constant factor is brought out by statistics. This fact is, however, bound up with so many conditions that it has little meaning taken by itself. The occupations and manner of life, together with the crowded dwellings of urban peoples, directly favor infection as contrasted with residents of the country; yet by absence of sanitation, country hovels may parallel the dangers in city tenements.

*Occupation.*—Certain dusty occupations especially predispose to tuberculosis. Stonecutters, quarrymen, metal and glass grinders and polishers are the most important. Organic dust is of much less importance, yet acts deleteriously to some extent upon millers, woollen and cotton weavers, cigar-makers, etc. *Noxious gases* also depress the health and irritate the air passages of smelters, chemists, and foundrymen. Extremes of heat and cold act similarly upon bakers, stokers, and plumbers. Ascher[2] has made a statistical and experimental study which indicates that smoke is also a directly predisposing factor, but the tuberculosis mortality statistics of the mill towns in America, such as Pittsburg, do not confirm this view. The *sedentary* employments, such as book-keeping, clerking, and other mental as distinguished from physical occupations, act more indirectly, by reason of long hours of confinement in a sitting or stooping posture, added to nervous strain. Out of 1947 private patients recorded with some occupation, the writer found 316 clerks and book-keepers, 147 students, and 97 teachers. The subject is so complicated with all the other things that make for ill-health that the prevalence of tuberculosis in any given occupation is not a certain index of the harmfulness of the calling itself. For example, persons of weak physique are more likely to select indoor sedentary employments which are not necessarily predisposing to vigorous persons. The excellent study by Lilian Brandt[3] summarizes the characteristics which make a calling appear to favor tuberculosis as follows:

"1. A low rate of wages, entailing discomfort and privations in the home.

"2. Unsanitary conditions of place of employment.

"3. Exposure to dust arising from marble, stone, plaster, wood, metals, or textiles.

"4. Excessive physical exertion or a continued constrained position.

"5. Close confinement within doors.

"6. Exposure to excessive heat.

"7. Temptations to intemperance.

"8. Long or irregular hours."

*Bad habits* contribute a most powerful predisposition. Alcoholic excess is a frequent history among the tuberculous who are otherwise free from predisposition. Tobacco and drug habits are less clearly predispositions, but

[1] An interesting theory promulgated by Surg.-Maj. Woodruff, U. S. A., is that blonde races who originate in higher latitudes become more susceptible to diseases, including tuberculosis, when transplanted to regions with strong sunlight, by reason of insufficient skin pigment.—*The Effect of Tropical Light on White Men.*

[2] *Der Einfluss des Rauches auf die Atmungsorgane*, 1905.

[3] *Handbook on the Prevention of Tuberculosis*, 1903.

lessen nutrition and the defensive powers. Masturbation, sexual excesses, and perversions favor infection by weakening the nervous energy and vascular tone. A considerable proportion of tuberculous males of good physique give a history of gonorrhœa and alcoholism. Irregular and insufficient sleep, extreme exertion, mental or physical, also coöperate with depraved habits to bring about the disease in many otherwise resistant individuals. Among the writer's cases 94 (5.5 per cent.) gave a history of dissipation alone, and 174 (10.3 per cent.) of overstrain, frequently combined with the former.

*Poverty.*—No single element in predisposition appears so important in the development of tuberculosis as this. Statistics of pauperism and consumption coincide in their variations; the causes that lead to poverty are potent in inducing this disease, and the consequences of poverty are yet more so, because crowding, squalor, poor and insufficient food, filth, and ignorance accompany the downward trend in humanity. Consumption is the social disease *par excellence* at the terminal stage of poverty. Körösi established for Budapest that among 10,000 living inhabitants, 40 well-to-do persons, 62.7 moderately well-to-do, 77.7 poor, and 97 paupers died of consumption. On the other hand, poverty as a *result* of family tuberculosis has not been sufficiently studied to make sure that such figures are not exaggerated.

**Danger of Infection.**—*Dwellings* which are crowded and poorly lighted and ventilated are the source of easy infection and form the chief danger to the poor in great cities. The "lung blocks" so graphically displayed by the New York Health Department and by the Phipps Institute in Philadelphia appear to show clearly how tuberculosis predominates in the most crowded sections of those cities. Besides the close contact of individuals, the air of the rooms is greatly vitiated, and the excessive heat and moisture debilitates the inmates. The classic experiments of Trudeau on the fatal effect of cramped and poorly ventilated quarters on tuberculous rabbits, as compared with the recovery of those permitted to live in the open, directly illustrate the baneful effects of crowding.

*Family.*—Tuberculosis is so largely a family disease, with from 40 to 60 per cent. of all patients disclosing a history of others in the household, that the importance of family infection can hardly be exaggerated. The opportunities are innumerable in the homes of the poor and rarely wanting among the wealthier classes. Apart from the usual delay in recognition of the disease where it progresses steadily to an advanced stage, there are many undetected pulmonary cases which become chronic or recover and masquerade under the names of la grippe, catarrh, bronchitis, asthma, typhoid fever, and malaria. These must be reckoned with in a study of family infection, and doubtless would swell the numbers materially. The danger to children is of first importance because of the ease with which infection occurs at this period of life; while adults are usually brought into a condition of susceptibility by illness, depressing care, and solicitude for the consumptive relative, besides the vicissitudes of life in general which fall heavily upon consumptive families.

*Marriage.*—The influence of marriage or of married life in relation to tuberculosis has been studied carefully, and the danger of infection of husband or wife appears relatively far less than for the children. It is obviously greater for the wife when the husband is the invalid, because the nursing is often a grievous burden in addition to other family cares, and

especially during childbearing and lactation. The husband, on the contrary, is usually away at work and a nurse or some other relative performs the duty. The percentage of cases due to infection between the partners in marriage is given as high as 23 per cent. by Cornet, but others attribute only 3 to 6 per cent. to mutual infection. Cornet's figures are from very poor people, the others from better-situated families. Mortality statistics have already been mentioned which indicated a generally higher death rate for widows and widowers from tuberculosis than for the single at those ages. Weinberg finds that the surviving partners of the tuberculous have twice the mortality from tuberculosis that is found in the general population at the same ages. Many other factors, however, play a part in such results, and the disease is actually less prevalent among the married than the single, "partly due to the fact that marriage in itself is more or less a process of natural selection, and partly to the greater regularity and soberness of life induced by marriage" (Mayo Smith).

*Factory or Shop.*—Formerly these places were nearly always unsanitary, poorly lighted, scantily heated, and without ventilation, all of which contributed to the danger of infection. In the large cities these conditions still prevail to a great extent, and the consumptive workman can unquestionably communicate the disease to his fellows if they are in close quarters and he is careless with his sputum. Cornet cites several instances of successive tuberculosis in factory employees. Clerks, salespeople, and employees in public offices where many persons congregate are not only exposed to their tuberculous fellow-employees, but to the indeterminable number of visitors who may bring the infection directly by coughing, spitting, or indirectly from their hands, handkerchiefs, clothing, etc. We may not believe, as Cornet states, that a consumptive workman is a greater danger to his fellow-workmen than to his family, for if he is so careless in his habits at work, he is likely to be so at home, where the far more susceptible children are exposed. On the other hand, it may well be true in the exposure of the child laborer, that disgrace of civilization the sum of whose disease and misery will never be fully known.

*Institutions, Sanatoriums, and Health Resorts.*—A great deal of divergent evidence exists for and against the danger of hospital infection for the employees, physicians, nurses, and attendants. Cornet relates that among the Catholic hospital nursing orders 62.88 per cent. died of tuberculosis in the cloisters during twenty-five years, according to a government inquiry, which included 74,306 persons. The conditions in America are apparently much better for nurses, although it is asserted that 10 per cent. of the medical internes of Bellevue Hospital have developed tuberculosis, and it is doubtless true of many other general hospitals where both nurses and physicians are in intimate contact with patients and under nervous strain from responsibility.

On the other hand, the record of special hospitals and sanatoriums for tuberculosis is quite the reverse, as in the case of the Brompton Hospital in London (Theodore Williams). Moreover, no case of tuberculosis has been known to develop among the employees of the Adirondack Cottage Sanitarium since its foundation, twenty-two years ago. These included waitresses, chambermaids, and laundresses, many of whom were badly nourished on entering the service. The same absence of infection among nurses and attendants was claimed by Dettweiler, of the Falkenstein Sanatorium.

From these contradictory experiences it is evident that there are marked differences in the hygienic conditions and control of the patients, whose habits largely depend upon their intelligence and station in life, or else entirely false inferences have been derived from incomplete data. Furthermore, the close confinement and devotional duties of the Roman Catholic sisters in Germany is to be contrasted with the greater freedom of the American hospital nurses, who are also selected in the main for good physique. In the consumptive wards of general hospitals the presence of bacilli has been repeatedly demonstrated in the dust, and Straus found them in the nasal secretions of one-third of the physicians, nurses, and other attendants at the Charité Hôpital in Paris. There can be no doubt, therefore, of the possibilities of infection in these institutions for susceptible individuals. It has been thought that the presence of tuberculous patients in general hospital wards endangered the other patients, and instances are cited in recent literature in which convalescing typhoid and pneumonia patients subsequently developed tuberculosis. While these have only the value of circumstantial evidence, the separation of consumptives from such patients is logically demanded.

Of late much fear has been excited about the danger of infection to the residents in *health resorts*. No foundation for such fear has been demonstrated in any American resort, and the most unbiased investigations have even proved the contrary, for relatively fewer cases of tuberculosis develop than among other communities not resorted to by the tuberculous. Several factors tend to obviate danger, such as the generally open-air life of the invalids, who are as a rule intelligent, and have comparatively little indoor contact with the residents. Furthermore, the disease is usually properly recognized and some precautions instituted, whereas these are often delayed at home or concealment is purposely practised.

*Prisons* and *asylums* have furnished a harvest of tuberculosis in the past. Villemin noted that the mortality from this disease was three times as great in the French prisons as among the free population. Quite similar records have held good for other countries. The deaths from tuberculosis in the Eastern Pennsylvania State Penitentiary from 1878 to 1902 were 60.8 per cent. of the total mortality (Hinsdale). In the New York State prisons 75 per cent. of the deaths were reported as due to tuberculosis in 1890 (Ransom). Cornet shows that there is greater danger in the penitentiaries than in the prisons where solitary confinement is enforced. It is far from clear, however, that contagion is especially frequent, since so many prisoners are already infected on admission, the confinement and depression of prison life developing the disease among a class especially prone to previous infection by their manner of life. Great improvement has been made in the construction and hygienic management of such institutions during the past ten years, and a corresponding decrease in tuberculosis has occurred in the more enlightened countries. The same is true for reformatories and institutions for the insane and imbecile.

*Schools.*—The question of school infection has received attention of late in increasing degree. Many teachers have the disease in an open form, and while their contact with the pupils is relatively less than that of the parents it constitutes a real danger. Because pulmonary tuberculosis is infrequent in childhood, the infection from fellow-pupils cannot be a frequent risk. Suppuration of lymphatic glands or bone tuberculosis may transmit the infec-

tion, but this also is a comparatively slight danger on account of the few bacilli in these discharges. Tuberculosis is, nevertheless, present in a large number of public-school children, as revealed by the modern inspection in vogue in some cities. In a recent investigation at Cleveland, Ohio, 7.5 per cent. of 504 children of tuberculous families or exposed more or less intimately to a tuberculous individual were found to have some form of the disease; 12.6 per cent. were suspected (Lowman).[1] Altogether, 20 per cent. of these children were considered in need of surveillance.

Grancher has discovered similar conditions in Paris. Among 4226 school-children 15 per cent. were deemed to be certainly tuberculous or strongly suspicious. The minimum estimates are appalling enough, but speak stronger for family infection than for the exposure in school.

**Infection.—Historical.**—The reference to the belief in contagion by Aristotle and Galen has been mentioned, and every century has had writers who recorded their opinions that consumption was infectious as well as transmitted from parents. The leaders in medical thought, Morgagni and Valsalva, excited the public fear to such an extent during the eighteenth century that drastic laws were enforced in Italy providing for isolation of consumptives, notification by physicians, and destruction of the clothing and effects of consumptives (Naples, 1788).

Similar dread of contagion prevailed in all the Latin countries, and it was customary to burn the clothing and bedding of consumptives in France, Spain, and Portugal. In fact, it was dealt with like a pest, as shown by the sad experience of Chopin, who was travelling in Spain in 1839; this is graphically described by George Sand in a letter written while travelling with him. The extreme unreasoning fear of contagion which was prevalent and still is a part of the folk-lore in southern Europe has reappeared in the bacterial era, fortified and exaggerated by half-truths in the minds of intelligent people.

During the early part of the nineteenth century the belief in contagion was lessened by the influence of Bayle and Laennec, who emphasized tuberculous diatheses, predisposition, and heredity, although admitting contagion in some instances. Then followed the development of microscopic study and a confusion of ideas as to etiology. The pathologists focused attention upon the morbid changes in the tissues and the inheritance of this disease became a firmly fixed belief among all classes of physicians. Virchow's teaching still further separated the idea of infection from tuberculosis because it uprooted the belief in the unity or specificity of tuberculous caseation and the identity of scrofulosis and tuberculosis. He believed in an inherited and acquired predisposition, which required no mysterious contagion to excite the disease. These ideas were dominant when Villemin's discoveries led to joint investigations by physicians to determine if possible evidences of infection. In America out of 500 physicians questioned by Holden in 1878, 250 replied, of whom 126 believed in contagion; but of the 10,000 members of the British Medical Association, Cornet states that only 1028 replied, and of those, 262 believed in the possibility of contagion—not a great showing of hands. Nevertheless, such inquiries were continued in other countries with more success, although the belief in heredity was predominant. When, therefore, Koch's discovery was announced, much attention was

[1] *Transactions of the National Association for the Study and Prevention of Tuberculosis*, 1907, vol iii

given to the possibility of the direct transmission of the bacillus from parent to offspring. Baumgarten has to the present time persistently maintained this to be the chief source of tuberculosis in spite of accumulated evidence for the importance of external infection.

The notable studies of Cornet next indicated the probable mode of infection to be from the dust of infected rooms and surroundings of consumptives; this formed the basis for the modern prophylactic measures for the disposal of sputum and disinfection of apartments. When the inhalation of sputum-dust had about achieved universal recognition in explaining infection, Flügge and his associates introduced strong experimental evidence of moist "droplet" infection, by which theory the predominant danger was attributed to the presence of a hard-coughing consumptive. Lastly, v. Behring has introduced the more revolutionary idea that in most cases the infection is derived from milk and begins in infancy through the intestinal channel, and is often from bovine sources. Amid all the confusion and readjustment of ideas in progress, it is small wonder that a general dread of any contact with tuberculous persons has steadily increased, in spite of definite knowledge of the sources of danger and the measures to combat it.

**The Sources of Infection.**—These are sufficiently well established to permit positive assertions to be made concerning them at present, though controversies are still being waged over the relative dangers of human and bovine tuberculosis.

The human sputum is the greatest factor in the dissemination of bacilli, whether by direct transmission in the moist condition or indirectly through the medium of dust in contaminated rooms, or of food, clothing, and other objects. Many millions of bacilli are contained in the consumptive's sputum and a large proportion of them are capable of growth when first discharged, judging from the culture experiments of Hesse with sputum directly upon agar and contrary to the former findings of Kitasato. On the other hand, the discharges from surgical tuberculosis contain very few virulent bacilli and are not conceivable as a frequent source of infection under ordinary conditions. Urine and fæces doubtless play some role indirectly through soiled garments and bedding, as well as the hands of the unclean, but in these cases the danger should be restricted chiefly to advanced invalids.

The milk and flesh of tuberculous cattle have long been regarded as sources of danger, but convincing proof of this has been difficult to obtain. That this is now entirely satisfactory may be confidently asserted. The sensational denial by Koch in 1901 of any serious importance from bovine infection for human beings led to an industrious study of the subject throughout the world and to the creation of two governmental commissions for this purpose, those of Germany and Great Britain. Both have rendered reports which confirm the earlier findings of Theobald Smith and Ravenel in the United States, who detected bacilli of bovine type in the mesenteric nodes of infants. The United States Bureau of Animal Industry has also conducted valuable experiments, all tending to show that bovine infection is not unimportant for man. Perhaps the most convincing proof thus far adduced is from the experiments of Fibiger and Jensen, who isolated cultures virulent for calves from two young children known to have received milk from cows with tuberculous udders, and in whose families no human tuberculosis existed. The value of the statistical studies on the frequency of bovine tuberculosis in man as gauged by the number of primary intestinal infections

has been doubtful in the absence of such culture and inoculation tests as the afore-mentioned. The number of cases with strongly presumptive evidence of bovine origin is nowhere so great as to compare in importance with the human source; but if it should later be demonstrated, as suggested by v. Behring, that the bovine type of bacilli may undergo a transformation of virulence by long residence in the human body, so that they are indistinguishable from the human types, the statement would require modification. That the milk and flesh of tuberculous animals are proved sources of human tuberculosis must be admitted, but obviously they are of varying importance according to the prevalence of the disease in domestic animals. In America bovine tuberculosis must be a relatively small factor in the causation of the human disease, because it is relatively infrequent, while in Japan it is entirely wanting, according to Kitasato, because not only is no milk used by the mass of people, but the few cattle in that country are free from tuberculosis. The same conditions concerning the use of milk are alleged to exist in Greenland (Djier), the Gold Coast (Fisch), China, the Philippines, Turkey, Sicily, and Sardinia; yet in all these countries tuberculosis is prevalent in all forms and to the same extent as in Europe and America.

On the other hand, it is thought to be of great moment in the British Isles and European countries by Raw, Woodhead, v. Behring, and others.[1] Tuberculosis in swine, sheep, goats, and the smaller domestic animals is a practically negligible danger, owing to the comparatively slight use of uncooked flesh and infrequency of the disease among them, as well as in the parts of the animal used for food.

**Hereditary Transmission.**—The ancient belief in the direct inheritance of the disease dies hard in spite of the weight of evidence against it as a frequent source. The direct transmission of tuberculosis involves the transfer of the bacillus in one of several ways: (1) From the father through the seminal fluid or by means of the spermatozoa; (2) from the mother through the ovum or placental blood.

Evidence for the paternal transmission rests on the positive findings of tubercle bacilli in the human semen and on certain experiments in which the testes of animals were inoculated (Gaertner, Cornet), or where bacilli were injected into the vagina before copulation (Friedmann). Since genito-urinary and miliary tuberculoses are infrequent and bacilli have not been found in the semen of ordinary pulmonary tuberculous patients the chance for paternal transmission is very small. Moreover, the experiments by Gaertner, Cornet, and others were unsuccessful on guinea-pigs and rabbits, while the successful results of Friedmann, who found bacilli in the young (eight-day) rabbit embryos, were obtained under entirely abnormal conditions; nor is there much doubt but that these embryos would have failed to mature. In fact, the experiments of Seige controvert those of Friedmann, as under similar conditions he obtained healthy progeny. The conception of an actual infection of the spermatozoa with the bacillus is quite out of the question from any facts in our possession. If bacilli succeed in penetrating the ovum from the semen. it is altogether probable that they must first infect the mother. In Gaertner's and Cornet's experiments genital infection of

[1] Yet Speck, after a collective investigation, states that only 27 per cent of 8010 adult consumptives in Europe were fed on cows' milk during the first three months of infancy.

the females occurred without producing disease in the offspring. All in all, there is no evidence, clinical or experimental, of a paternal transmission in the sense of inheritance. The infection of the ovum is equally doubtful before impregnation, although Baumgarten claims success in one rabbit's ovum artificially fecundated. The well-known experiments of Maffucci, who inoculated 19 hens' eggs and hatched 9 delicate chicks which died soon, some having evidence of tuberculosis, are not exactly applicable to mammals. It is more than likely that human ova in which tubercle bacilli might lodge would be unfruitful. Clinically, ovarian and tubal tuberculosis is uncommon and a complication which usually interferes with impregnation.

*Placental transmission* is practically the only form of inheritance which merits attention, and this is, strictly stated, congenital infection from the mother. Exhaustive search has been made for cases of tuberculosis to support the inheritance theory and a list of twenty has been collected by Schlueter which are considered to have been undoubtedly derived from intra-uterine infection. Schmorl and Kockel reported the first cases of placental tuberculosis associated with disease in the child in 1894, and many pathologists have added cases which are more or less doubtful. Confusion with congenital syphilis was frequent and easy, so that the only definite proof has been by inoculation of portions of placental or fœtal tissues or the demonstration of the tubercle bacillus by staining; thus the actual number of observed cases is really very small in man, although it has been found more frequently in late years. It is also comparatively more frequent in cattle (Schlueter collected 70 cases). Warthin and Cowie have made a special study of placental tuberculosis. Not infrequently the bacilli have been demonstrated by inoculation with the fœtal tissues when no signs of tuberculosis were evident in them; this has been used by Baumgarten as an argument in favor of his well-known theory of latency and insusceptibility of the infant tissues to the formation of the tubercle, owing to their great activity of growth. Experimentally, the question of inheritance from the mother has been studied extensively. Gaertner's positive results are frequently quoted in support of the inheritance theory, but he inoculated female white mice with large amounts of tubercle bacilli which they are now known to harbor in the blood more than other animals (Roemer). On the other hand, Sanchez-Toledo, Cornet, and Hauser obtained only negative results in numerous inoculated guinea-pigs and rabbits whose young were in turn used to inoculate other animals. Even intravenously inoculated rabbits rarely transmitted the bacilli.

The methods by which intra-uterine infection can occur are by the direct passage of bacilli from the blood of the mother to the child through a rupture in the vessel walls of the villi or by means of an actual placental focus from which bacilli may escape into the fœtal circulation. Cornet discusses this mechanism with especial fulness, but considers the transfer of bacilli only exceptional; being possible solely in cases of far-advanced or miliary tuberculosis in the mother, which results in abortion or a short-lived infant, should it reach full term. He argues very properly that if bacilli can traverse the placental wall, the toxins must also pass through and injure the fœtus. The claim of Baumgarten for inheritance of the parasite and a dormant stage in its life-history is well combated by the relatively few cases where the conditions are present for transmission of the bacilli and the acute course of infantile tuberculosis in general. Among 1005 surgical tuberculous

patients between the ages of ten and fifteen, Lannelongue found only 3 whom he could denominate congenital. Since the opportunity for external infection begins at birth in just these supposedly hereditary cases, we are not justified in regarding them as such; nor can we consider the inheritance of the bacilli an important factor in the conveyance of tuberculosis from parent to child. Atavistic inheritance of the bacilli from the grandparents is wholly inconceivable.

**External Modes of Transmission.**—The opportunity for receiving tubercle bacilli into the body from outside begins with birth and the means of transmission are numerous in infected surroundings. Cases are on record where consumptive midwives are supposed to have infected infants by blowing into the mouth to start respiration at birth (Cornet). Inoculation experiments with the milk of consumptive mothers have been generally negative, as would be expected, since actual disease of the mammary gland is rare. Yet breast-fed infants can readily get the bacillus from sputum-soiled fingers of the mother which are frequently in contact with the nipples or put into the infant's mouth. The same is true of the bottle-fed nursling apart from the danger of bovine sources of infection. Perhaps next in importance are the fingers and toys of the creeping infant, frequently soiled, as they certainly must be in the dwellings of the consumptive poor, from infected dirt of the floor as well as from the clothing, and especially the handkerchiefs of the consumptive mother or nurse. Bacilli have been found to be frequent on the hands (Dieudonné) and under the nails (Preisich and Schutz) of children in consumptive families. The use of handkerchiefs to receive the expectorated sputum or to wipe the mouth is quite universal among otherwise cleanly persons, and unquestionably constitutes a potent means of transmission, both in the moist condition and after drying. Contamination of the pocket, dress, or pillow is frequent by the customary method of handling handkerchiefs, but particularly affects the hands of the patients (Baldwin).

Bacilli are decidedly more virulent in the moist condition, and it is conceivable that the hands may convey them frequently from the parent to child indirectly by food, confectionery, drinking cups, doorknobs, pencils, etc. The frequent use in common of spoons, forks, glasses, towels, etc., is also to be recalled. The contamination of food is also possible by means of the feet and excrement of house flies which have previously alighted on sputum (Spillman and Haushalter, Moeller, Lord); also by cockroaches (Kuster) and lice (Weber).

Sputum may be brought into houses on shoes and trailing garments, and by pets, especially dogs, which habitually lie upon the sidewalks and doorsteps; also, they may convey infection to children by their habits of indiscriminate licking. It is an open question whether the inhalation of sputum dust from floors and clothing and the moist spray from the cough constitutes the most serious danger in childhood. The deep inspirations of the crying infant give the opportunity, it is true, but the dose of infection in this form is likely to be less than in the other modes.

We know through the numerous examinations of dust that it is a means of transmission, but the bacilli have but limited vitality when dry, and as new conceptions of infection have come to view the role of dust diminishes in seriousness. The demonstration by Flügge that moist particles of sputum were coughed out so impalpable as to float in the air some minutes and could be inhaled brought out a factor formerly recognized by Cornet in

his experiments, but not sufficiently valued. In view of the remarkably ingenious experiments which support each side of the controversy between these experimenters we must assume that both modes of infection are of some importance. The danger of so-called droplet infection results chiefly from expulsive coughing, but may occur in hawking, loud talking, laughing, singing, and sneezing. Ordinary breathing carries no infection, as many experimenters have shown.

How little danger there is for adults even when directly exposed to the cough, spray, and dust is shown by the investigation of Saugman. Among 174 previously healthy sanatorium physicians whose average service was three years and who were followed three and a half years further, but 2 developed tuberculosis; also among 64 laryngologists from eight clinics none were affected during or after their service. Considering the close contact with patients and frequent demonstration of bacilli on the head mirrors and even in the nasal mucus of physicians (Straus, Moeller), the record is noteworthy and evidence against the frequency of adult infection as well. The act of kissing on the lips is not only unsanitary, but may be a danger to children, though for adults this is probably overestimated in the popular mind.

Some other means of transmission are suggestively possible, but of exaggerated importance in the lay mind as far as evidence goes. Such are the blankets of sleeping cars; telephone transmitters; money, particularly paper currency, and library books (Mitulescu). It may be admitted that in some instances young children are endangered in these ways, but it is altogether doubtful that adults undergo danger worthy of mention.

**Paths of Infection.**—It has been customary to consider three distinct modes of primary infection in tuberculosis apart from inheritance, in accordance with former theories of the reception of the bacillus into the body. These were by (1) inoculation, (2) inhalation, and (3) ingestion. Since changed conceptions have been introduced and the probability that combined inhalation and ingestion make the mode of infection from the exterior less simple than the above division implies, it seems more useful to make the distinction only between the three kinds of surfaces exposed to invasion from without, namely, (1) the cutaneous, (2) the mucous membranes, and (3) the pulmonary alveolar. By this division all sources of infection are recognized and included without undue emphasis being placed on any one mode. That it has not been a simple matter to establish the exact path of entrance of the tubercle bacillus into the human body is evidenced by the mass of experimental work devoted to the problem through many years, out of which disputes and confusion have arisen and still reign.

*Cutaneous Inoculation.*—Infection through the external skin is of slight importance in the production of generalized tuberculosis. The conditions are not favorable for an easy proliferation of tubercle bacilli in the skin itself, possibly because of deficient nutriment and the insusceptibility of the skin epithelium. The mere rubbing of tubercle bacilli into the skin is insufficient to infect adults, but abraded surfaces, especially in children, are occasionally the starting points of fatal infection. Inoculation tuberculosis is for the most part localized at the site of the wound or at most spreads only to the nearest lymph nodes. It is seen frequently on the hands of pathologists and bacteriologists who have to do with tuberculous material and experimentation, and it is surprising that more serious results do not follow.

Laennec himself, in 1799, received an inoculation on the hand and died of pulmonary tuberculosis twenty years later. It is doubtful from the evidence available that there was any causal connection between the two events, although Villemin cited this as an illustration of the inoculability of tuberculosis, and v. Behring has recently declared himself in favor of this theory of Laennec's case, in conformity to his belief in the slow development of the disease. Nevertheless, man is certainly quite resistant to cutaneous or subcutaneous infection, considering by contrast the ease with which susceptible laboratory animals develop progressive tuberculosis from slight inoculations into the skin. Many instances of cutaneous inoculation are recorded in the literature, some of which may be enumerated here: The cuts from broken cuspidors and chamber vessels; from ear-rings; from splinters in an infected floor into bare feet; from the operation of tattooing; in performing circumcision; from scratches in scabies and eczema with infected fingernails; also of the nose and by the use of handkerchiefs previously used by consumptives. Bruns has collected five cases produced by hypodermic injections, three of whom were morphine habitués (Cornet).

Infection of the nasal fossæ and corners of the mouth and eyes not rarely leads to lupus of the face; many of these lupous subjects also have tuberculosis elsewhere which is the source of the infection. Autocutaneous infection is rarely produced, considering how frequently the hands and nails are soiled with sputum. One case seen by the writer was that of a consumptive seamstress who had infected her forefinger with her needle, which she was wont to put into her mouth. Subsequently, her wrist-joint became involved, presumably from the infected finger.

Vaccination was formerly regarded as a possible source of danger from the inoculation of tubercle bacilli with the human lymph, but the modern use of calf lymph with the precautions taken in its preparation leaves no basis for fear. Calves employed for producing vaccine are selected free from tuberculosis by the tuberculin test. Moreover, the experiments of Carini indicate the improbability of the lymph containing tubercle bacilli even when prepared from tuberculous animals.[1] The comparatively mild effects of accidental or intentional subcutaneous inoculations (Baumgarten, Klemperer, Kleine) with bovine bacilli have been used as proof of the relative harmlessness of bovine bacilli for man with questionable propriety, in view of the fatal results of such infection through the intestinal channel, and the instances of even progressive disease ascribed to skin infection (Ravenel). The ultimate outcome of the bold self-inoculations in the arm with virulent bovine bacilli, in the case of both C. Spengler and Klemperer, should be a source of anxiety, although a real contribution to science.

*Mucous Membrane Infection.*—When the number of mucous surfaces exposed to agencies from without the body is considered, it may at once be suspected that the tubercle bacillus finds entrance most frequently through the many wounds and abrasions of the orifices of the body, or by absorption from the upper respiratory and gastro-intestinal tract, whether inhaled or ingested with food.

*Primary inoculation tuberculosis* is nevertheless not often recognized, if indeed it occurs frequently, as believed by some, from abrasions in the mouth

[1] The possibility of skin inoculation from the bites of insects, such as house flies and bed-bugs, which may have ingested sputum may be admitted, especially in the case of children when asleep, although actual proof is wanting of this means of infection.

and tongue, such as are produced by carious teeth or after their extraction, and following operations upon the nose, nasopharynx, larynx, and tonsils. Still rarer are instances of genital, rectal, and conjunctival infection from injuries. It would be surprising how infrequently infection apparently results from lacerations in the mucosa, which leave an open door for tubercle bacilli with conditions favorable for absorption, were it not evident that the virus is not universally present and not always in a virulent condition.

In youngest infancy and childhood, however, abrasions of the gums in dentition and the coincident transport of bacilli from dirty fingers both of the child and mother into the mouth may lead to infection, as emphasized by Volland and Westenhoeffer. The same is true of the habit of picking the nose. How often infection actually occurs in these ways has never been ascertained, since it is well recognized that the portal of entry may not show signs of disease, especially in infancy. Furthermore, the assumption formerly made as an axiom by Cornet and others, that the nearest lymph nodes to the pathway of infection would always first become diseased is now seriously questioned. The experiments of Weleminsky, Harbitz, v. Behring, Bartel, and others, in which living tubercle bacilli were demonstrated by inoculation of lymph nodes into guinea-pigs when no signs of disease were present in the nodes, indicate the possibility of an unsuspected path of entrance, especially in children in whom no trace may be seen at the site of infection. On the other hand the objection made that sooner or later the regional nodes would show the disease if infection really occurred, is a strong one, and on this basis statistics of lymphatic tuberculosis about the face and jaw do not favor great frequency for traumatic infections in those regions.

When not strictly construed, inoculation tuberculosis applies to infection through the mucosa whenever a deficiency of epithelium is produced, whether by injury or disease. It is nevertheless quite as accurate to consider this as *infection* by *absorption*. The readiness with which the glandular and especially the adenoid tissues of the nose and throat become the seat of transient infections has long furnished an argument in favor of this pathway also for tuberculosis (Aufrecht, Freudenthal). Moreover, in the situation of the postnasal and faucial tonsils with their crypts and fissured surfaces, their frequent hypertrophy and loss of epithelium, there is abundant opportunity for the lodgement of inhaled or swallowed bacilli. When pulmonary tuberculosis is present, secondary disease of the faucial tonsils is very common, yet primary tuberculosis of these structures is comparatively rare.

Jonathan Wright, Broca, and many others have made microscopic examinations of "adenoids," with generally negative results. Cornet's summary of 1745 cases gave 4.1 per cent. of positive results. Primary tuberculosis of the faucial tonsils is less rare, but closer observation of late and inoculations of all these tissues have revealed latent bacilli present more frequently than hitherto suspected (Dieulafoy, Lartigau and Nicoll, Harbitz).

The statistics of primary tuberculous cervical adenitis or pronounced "scrofula" have hitherto been taken as a fair index of the frequency of infection through the upper air passages and mouth, and more particularly through the medium of the tonsils, but the proportion is far below that of supposedly primary disease of the bronchial nodes. Submaxillary and

cervical nodes are so frequently enlarged in children from pyogenic infections that the decision as to the frequency of primary tuberculous infection of this lymph system is by no means easy.[1]

This fact demands more attention because of the more important studies in recent years (MacFadyean and McConkey, Spengler, Walsham, and others, but especially by Harbitz), which by more careful microscopic examination combined with inoculation tests have disclosed the fact that lymph nodes presenting nothing but simple hypertrophy or even normal appearances may contain virulent tubercle bacilli without other evidence of tuberculosis. It is disquieting to note that Harbitz found them most frequently (13 out of 18 cases) only in the cervical group of nodes and in the youngest infants, mostly less than a year old. These are significant facts bearing upon the absorption of bacilli from the mouth and nasopharynx. Whether lodgement or retention of tubercle bacilli in these nodes for a time necessarily implies infection or not is a question yet more difficult to decide. Moreover, it is unexplained as yet why pigmentation of the cervical nodes does not occur, as in the bronchial system, from the absorption of dust, if bacteria are so readily taken in by the emigration of leukocytes outward and inward on the surface of the tonsils. Nearly all the dust that is inhaled is caught in the nose, or, during mouth-breathing, in the mouth or pharynx. The coarser particles of dust are soonest deposited and normally cast off by the mucous flow and movement of cilia in the nose or frequently swallowed from the pharynx. Relatively little reaches the larynx, trachea, and bronchi by direct inhalation or is aspirated secondarily from the nasopharynx and mouth.

Localization of tubercle bacilli in the mucosa of the lower respiratory tract is rare as a primary disease so far as pathological studies have revealed, although it is by no means certain that bacilli do not frequently pass through into the adjacent lymph nodes and produce the first recognizable changes in the lung hilus and bronchial nodes, leaving no trace on the mucous surface. Slight erosions of the laryngeal epithelium are so common that the chances for primary infection on such sites should be frequent, yet careful study has revealed only isolated cases. The paucity of such observations both in the trachea and bronchi has been a favorite argument against the pulmonary inhalation theory of tuberculous infection, but a most valuable study by Abrikosoff brought to light 8 cases in 453 adults dying of other diseases, in which beginning tuberculosis was demonstrated in the walls of small bronchi and involving only the mucous membrane and excluding all sources of the infection except inhalation.[2]

The gastro-intestinal tract has been brought to the front in recent years as the most important pathway of entrance for the tubercle bacillus. While a few pathologists long ago held to the idea of ingestion infection from their successful feeding experiments, the weight of evidence seemed

[1] Volland estimated that 94 per cent. of children between the ages of seven and twelve years had enlarged cervical nodes. Neumann summarized 4883 children between one and nine years, of whom only 6.38 per cent. had presumably tuberculous enlargement of the nodes, while Laser considered 32.4 to 58.9 per cent. of cervical enlargements tuberculous in 1216 school-children.

[2] The difficulties in such examinations are well indicated by Schmorl, who found only 42 cases in 4000 where a decision could be made as to the starting point of infection in the lung; in only 10 of these was the disease confined to the bronchial wall.

to be in favor of lung infection. Nevertheless, v. Behring aroused the question anew in 1902 by announcing his conviction that food infection accounted for all the results of previous experiments, questioning the validity of Cornet's and Flügge's interpretations, and presenting his own observations that lung tuberculosis was primarily of intestinal origin and from infected milk. This revolutionary idea has found slow acceptance, but has led to many new experiments with partly confirmatory results and to a pronounced modification of the theory of primary infection by way of the pulmonary alveoli, since careful pathological studies have been made of the earliest signs of infection in the lymphatic system (Harbitz, Weichselbaum, Mallory and Wright, and others). It is only necessary to mention here that v. Behring and Roemer have demonstrated the easy permeability of the stomach and intestinal mucosa of the newly born animal for bacteria and unchanged proteid. This they regard as the time of greatest danger from tuberculous infection in the family, and the condition is ascribed to incomplete development of the gastro-intestinal epithelium and digestive ferments. Later in life the passage of bacilli is favored by erosions due to catarrh or other abnormal conditions and diseases. The bacilli may pass directly into the blood through the thoracic duct or be arrested in the mesenteric nodes in primary infection without a trace of their site of entrance, but they tend to localize in the mucosa and Peyer's follicles if a previous infection has created a susceptibility. Baumgarten maintains that a focus is always produced sooner or later at the point of entrance, although it may be microscopic. Many recent experiments have shown that the bacilli can pass into or between the intact epithelium and can be traced step by step to the mesenteric nodes or thoracic duct, chiefly from the lower part of the ileum or cæcum; the stomach is rarely penetrated except in newly born animals.

The demonstration of primary mesenteric node infection in young infants, and adults as well, without other signs of the disease (Harbitz), leaves no doubt of the possibility of intestinal infection under some conditions. The only questions at present mooted are: (*a*) Their frequency compared to the respiratory route; (*b*) the relative number of bacilli needed, *i. e.*, the dose, since Flügge claims to have shown that vastly more are required in feeding experiments than by inhalation; (*c*) finally, the important matter of its relation to pulmonary tuberculosis is yet unsettled.

Infection of the genito-urinary tract and conjunctiva is, so far as known, or at least proved, of traumatic origin when from the exterior and too rare to deserve special consideration.

*Pulmonary Alveolar Infection.*—In spite of the somewhat modified conceptions of the pathways of infection, the belief in the reception and absorption of tubercle bacilli through the delicate epithelial walls of the pulmonary alveoli persists.

The most important fact in favor of this theory is the presence of pigment in the cells themselves or in the interstitial spaces, especially under the pleural surface. The convincing experiments of Arnold remain to-day the chief foundation for the inhalation theory, in spite of attempts to show that pigment can be deposited in the lungs after feeding experiments (Vansteenberghe and Grysez).[1] When carefully controlled, such experiments have produced quite opposite results (Bennecke, Aschoff). Hence, the deposit of coal-dust and stone-dust in the lungs of miners, etc., cannot be interpreted at

[1] *Annales de Institut Pasteur*, 1905, vol. xix.

present in any way but by inhalation directly into the alveoli or small bronchi. It must follow logically that the bacilli in the form of fine dust must also lodge there and be carried into the subpleural and interstitial spaces, as is true of anthracosis. The problem seems simpler at first sight than it really is, because the very earliest changes in the inhalation infection experiments are not usually in the alveoli, but in the lymph nodes, probably from mucous membrane absorption, since obviously less inhaled dust or spray penetrates as far as the alveoli. Moreover, the great frequency of bronchial lymph-node tuberculosis before any discoverable changes in the lungs, especially in children, and the greater permeability of the lymph spaces at that age have thrown doubt on former theories of the mechanism of primary infection. It is especially since v. Behring has called attention to the fact that subcutaneous inoculations anywhere into the lymphatic system, such, for example, as under the tongue, can lead to typical pulmonary tuberculosis identical in appearance to that produced by inhalation that a new aspect of the problem demanded attention. This mode of lung infection is accomplished by way of the bronchial glands in most cases which receive the lymph from a large area and pass it into the blood very directly, thus carrying the infection to the small capillaries in the alveoli, where they lodge. These observations have received ample confirmation and indeed were not novel, but hitherto had escaped emphasis. This renewal of attention has brought out many ingenious experiments, conspicuous among which are those of the United States Bureau of Animal Industry by Schroeder and Cotton, Calmette and Guérin, Weichselbaum and his pupils, Bartel, Newman and Spieler, while the defenders of the inhalation theory (Cornet and Flügge) have repeated their experiments with precautions to exclude paths of infection other than the lung. It is impossible to give space to the many points in the controversy, but enough may be mentioned to show that primary alveolar infection is possible in various ways, including inhalation. Hodenpyl, in 1899, decided that the subpleural pigmented nodules so frequently found were often tuberculous when no other focus was discoverable, and Ribbert has recently accepted the same view, but thinks the deposit of pigment generally precedes and aids the retention of tubercle bacilli by clogging the lymph spaces and minute subpleural lymph nodes. The frequency of tuberculosis among stonecutters strongly supports this view. In contrast to this are the observations of Wainwright and Nichols, who examined the lungs of coal-miners and conclude that the connective-tissue growth stimulated by coal-dust acts as a protection against implantation by tubercle bacilli, thus accounting for their relative immunity.

Moreover, Schroeder and Cotton have ingeniously produced pulmonary tuberculosis in calves by inoculations into the tail as well as by feeding experiments. It is therefore maintained that the lung capillaries act preeminently as a filter for the blood and lymph circulation, and indirect infection frequently occurs by way of the intestine, mesenteric nodes, or thoracic duct, thence to the blood stream and lungs.[1]

A modified opinion is therefore necessary at present in reference to the frequency of directly inhaled primary infection of the alveoli, in that it is less frequent than formerly supposed.

[1] It is even argued by Weleminsky that a reverse lymph flow from the bronchial nodes to the lung periphery accounts for many cases supposed to be primary alveolar inhalation tuberculosis.

**Relative Frequency of Modes of Infection.**—As there is a general agreement that infection through the external skin is not of much moment except in infants, the statement that it forms but a fraction of the whole number is justified. Much disagreement exists about the other avenues, however, more especially as to the lung and intestine. The weight of opinion was in the past in favor of the lung because the statistical comparisons of cases of supposedly primary lung and bronchial node disease were far in excess of those in the intestine and mesenteric nodes. The estimates vary greatly, however, ranging in the case of primary intestinal invasion from 2 to 30 per cent. Such differences were largely due to the failure to make a careful study of the very incipient stages or latent forms in the lymph nodes on the part of the older observers and the absence of microscopic and inoculation tests. When the later work of Councilman, Mallory, and Pearce, Harbitz and Rosenberger is examined it is seen that the bacilli are much more frequent in the mesenteric nodes than was supposed. How often they go on to the production of actual disease may still be an open question. At present the figures suggest that one-fourth of all cases of tuberculosis, in children at least, receive the infection by way of the gastro-intestinal route, either simultaneously with or independently of other ways of entrance. A considerable proportion of primary infections through the upper air passages have also been overlooked in the past because no special attention was paid to the cervical nodes, and no estimate can at present be made of their frequency. Therefore, due allowance must be made for these in reckoning the number of primary bronchial node cases, so that altogether the knowledge now available tends to lessen the importance of primary inhalation infection through the bronchi and alveoli, yet by no means places it second to other channels. There is some reason to think that below the age of fifteen years infection by other channels is more frequent and perhaps preponderant by way of the digestive tract, and localizes in the lymph nodes at first; yet the possibility of simultaneous inhalation and ingestion infection prevents a certain conclusion. In adults the first focus of disease is more often at the portal of entrance, which supports the inhalation theory for the origin of pulmonary phthisis in the majority of cases, whether it be primary or so-called "superinfection." Furthermore, the greatest proportion of latent or healed tubercles found in the lung apices coincides with the increased age of such individuals and is best explained by inhalation infection.[1]

**Latent Infection.**—This expression is intended to apply only to the presence of the disease-producing agent in the body without actual tubercle formation, a true "pretuberculous" stage of the disease.

Baumgarten has long stoutly maintained that bacilli could be inherited and rest for long periods in the body, restrained by the active tissue growth of the infant. There is little reason to think this to be true, as already explained. Tubercle bacilli have been found in the lymph nodes without apparent effect on them except to produce a slight hyperplasia; at least,

[1] Von Behring maintains that secondary tuberculous infections tend to localize at the point of entrance because of a susceptibility acquired from the first infection, thus accounting for ulceration in the lung and intestine found in adult life. He believes that the condition of susceptibility corresponds to that known as "scrofulosis" when well established. This theory needs extended observations to confirm this explanation of the phenomenon, but has an experimental basis and clinical support in the greater frequency of superficial ulcerations in adults as compared with children, and the large number of persons who show susceptibility to tuberculin.

specific changes may be absent for some time (Loomis, Manfredi and Frisco, Harbitz, etc.). Bartel and Neuman, by means of feeding experiments in rabbits, found that living bacilli could be present one hundred and four days in the nodes without specific changes, and finally disappear without leaving traces. Cornet thinks, however, that no prolonged latency is possible and ascribes these results to mild infections with weak bacilli which do not gain a hold in the body, while v. Behring regards mild infections in childhood as predisposing or immunizing to later infection according to their severity. From what is known of the biology of the bacillus the probabilities are that virulent bacilli go on to growth and tubercle formation within a few weeks, and that less virulent strains may remain alive several months and eventually die out with or without traces of their presence being left. In the absence of evidence to the contrary it must be assumed that in the instances of prolonged latency of the disease itself, which are so frequent, the bacilli must slowly multiply at times, or assume a dormant stage unknown in artificial culture.

**Reinfection.—Cumulative Infection.**—In an individual previously infected with tuberculosis we know that tuberculin susceptibility may exist for a long time after clinical healing has occurred.

It is, therefore, of interest to know whether such persons are capable of further infection from a source outside the body. The matter is very difficult to investigate and the proof quite circumstantial when relapses in healed pulmonary tuberculoses are referred to a fresh infection. Experimentally reinfections are not easily produced in animals, yet successive infections are usually assumed to have occurred in persons who have had a history of healed lymphatic tuberculosis in childhood (Cornet).

If future experiment and observation shall demonstrate that a primary infection is sufficient to account for the source of all subsequent developments of the disease, which position v. Behring now holds, it would be more in keeping with the results of experimental immunity studies. On the other hand, cumulative infection in tuberculous families seems impossible to deny in young children under repeated exposure.

**Frequency of Infection in General.**—As to the frequency of tuberculous infection in general, Naegeli's remarkable findings of 99 per cent. in 500 autopsies, and those of Burkhardt, who found 91 per cent. in 1262 sections, are doubtless too high for the general population, since the material was taken from hospitals in manufacturing cities (Zurich and Dresden). Further objection is made that many of the cicatrices, adhesions, and chalky foci assumed to be remains of tubercles were in reality not such or may have been caused by dead and weak virulent bacilli. Inoculations of calcareous nodules do not prove positive infectivity as a rule (Kurlow, Weber), even when the microscope reveals bacilli present. L. Rabinowitsch was successful in 5 cases, but considered the virulence weaker than normal. The percentages estimated by most pathologists, who usually regarded only gross appearances in determining tuberculous foci, vary between 30 and 60 per cent. of all sections. Probably the recent estimate of Harbitz from 50 to 70 per cent. for all ages represents an approximation of the truth in a matter the decision of which is of unusual difficulty.

An effort has been made to reach conclusions as to the frequency of tuberculosis by the tuberculin and agglutination tests. While the figures obtained by Beck (tuberculin) and Romberg (agglutination) correspond in a general way to postmortem findings, too many disturbing factors impair their value.

**Summary of Present Views on Infection.**—It is highly desirable to arrive if possible at some definite conclusions from the mass of facts now at our disposal and compare them in relative importance. In the first place the doctrine of inherited or acquired susceptibility still holds sway except that a specific susceptibility is in doubt and at most not common; next, that all infants are susceptible, and that susceptibility lessens with increasing age; lastly, that adults are comparatively insusceptible when without general or local lowered resistance and repeated or prolonged exposure. As to the sources of infection, the consensus of opinions and ascertained facts point to the sputum as of overwhelming importance, and that in certain cases, and especially in restricted areas having a large percentage of tuberculous cattle, cows' milk is an important factor, the flesh of tuberculous animals being of minor importance; lastly, that the mother's milk, the urine, fæces, or other excretions of tuberculous individuals are not frequent sources of the infection. In the means of transmission there is a growing belief in the greater importance of infected food—especially milk—for infants and childen rather than for adults; that the food may be infected directly by coughing or by dirt and dust from the floor and hands; that fingers and many other objects that find their way to a child's mouth are dangers. To adults both dust and moist droplets are the direct carriers of infection more often than infected food. It is doubtful whether inhaled dust is as dangerous as formerly supposed, but equally doubtful that the coughed spray plays a greater part than dust when the menace to adults is being considered. Infection is not often received through the skin, but most frequently through the mucous membrane of the mouth, air passages, and intestine. Alveolar lung infection is doubtless primary in some cases, but is being relegated to second place by some, in comparison with the upper air passages and digestive tract. Pulmonary tuberculosis is often secondary to the latent lymphatic form contracted early in life. The infection may be dormant a few weeks before exciting the formation of tubercles, may then die out and leave no trace, or progress to the stage of actual tubercles, and finally after a prolonged incubation stage in the lymphatic apparatus become distributed to various organs. It is uncertain that a second infection from outside the body is of frequent occurrence after clinical healing of pulmonary tuberculosis in adults; 50 per cent. of the general population acquire an actual implantation of tubercle bacilli at some time during life.

**Secondary Auto-infection by Tubercle Bacilli (External).**—When tuberculous foci ulcerate or burst through the epithelial layers the opportunities for further spread of the disease are enormously increased in spite of the possible relative immunity acquired by the lymphatic system. As already mentioned this relative immunity may indeed favor the arrest of the bacilli in the skin and mucosa from the hypersusceptibility acquired, and thus lead to the great frequency of secondary ulcerations on the surface. Considering how numerous the bacilli are in the sputum it is not strange that the extension of the disease in the lungs should be attributed largely to secondary infection both of the alveoli and small bronchi from an older focus ulcerating into the lumen of the air passages. In the same way the foci in the larynx, tonsils, and intestine are the frequent sequelæ of ulcerative phthisis, thus making the decision about the primary pathway of infection practically impossible in advanced tuberculosis.

# CHAPTER VIII.

## THE PATHOLOGY OF TUBERCULOSIS.

By W. G. MacCALLUM, M.D.

**The Effects of the Tubercle Bacillus on the Tissues.**—The action of the tubercle bacillus on the tissues is in its essentials similar to that of most other infectious agents which give rise to inflammatory processes, and it seems that rather too sharp a line of distinction between these anatomical effects and those of other inflammatory irritants has usually been drawn. Nevertheless, the changes are sufficiently characteristic to be recognizable with a fair degree of certainty which is rendered complete by the demonstration of the bacilli in the tissues. The anatomical changes are not uniform, but may present rather widely different appearances according to the mode of invasion and virulence of the bacilli. All such altered tissues have, however, in common the tendency to undergo a type of necrosis with the formation of a caseous material.

Perhaps the most characteristic of the results of the invasion of the tubercle bacillus is the formation in the tissues of minute grayish and translucent nodules of firm consistence, the miliary tubercles, so called from their resemblance in size to a millet seed. So characteristic, indeed, were these thought to be that the disease and the bacillus naturally received their names from this circumstance. Such nodules vary a great deal in size, and it now appears that those which are truly miliary, that is, resemble a millet seed in size, are by no means the smallest or ultimate tubercles, which may be so small as to be just within the limit of vision of a practised eye. This variation is in some degree dependent upon the tissue involved, the most minute tubercles being frequently seen in the liver, while those in the spleen and kidneys are usually larger. They may occur embedded deeply in the substance of solid organs, scattered upon the surface of such organs, in the lining of cavities, or in the walls of vessels, or they may form part of a sort of granulation tissue which results from the activity of the bacilli. The tendency to their formation is very strong, so that in the tuberculous lesions which are apparently not of this nodular character, especially after they have reached the later stage in their development, abortive attempts at the formation of such circumscribed nodules are always recognizable, new tubercles being formed as the old ones are destroyed and merge into the caseous material.

In their fresh condition the tubercles are visible, or often more readily palpable, as rounded or ovoid or flattened granules firmer than the surrounding tissue, and pearly gray or at times almost entirely translucent. They may be scattered singly, but more frequently they are grouped together or coalescent in such abundance as to encroach very greatly on the surrounding tissue. The translucence of the small tubercles persists for no great length

of time, for within a short period, usually two or three days only, after their formation a central spot of opacity, usually of grayish or yellowish-white color, appears which gradually increases in size, and when adjacent tubercles coalesce becomes confluent with that in the next nodule. This opacity indicates the beginning of the ultimate necrosis or caseation which so generally befalls the tubercles. Fresh miliary tubercles are, however, frequently found at autopsy, since their formation in most cases is a more or less continuous process, new crops of nodules appearing as the result of dissemination of the bacilli from the older foci. In certain instances—and these are the cases of *acute generalized miliary tuberculosis*—thousands of such tubercles appear simultaneously not only throughout the lungs, but thickly scattered throughout all the organs and tissues of the body, studding the surfaces, and roughening the cut surface of every organ by their prominence. These thousands of tubercles usually result from the wholesale introduction of the bacilli into the blood stream from an older focus which invades a vein or the thoracic duct, and the patients die before the individual tubercles have had time to undergo much alteration.

Finally, such minute tubercles may under certain conditions remain more or less translucent, and without undergoing any caseation become converted into firm fibroid nodules in which the characteristic structure of the fresh tubercle is lost and only a hyaline mass of dense fibrous tissue remains. This may be regarded as a process of healing..

Microscopically, the miliary tubercle in its fully formed state is composed of a roughly concentric mass of cells of elongated form, with long, oval, vesicular nuclei. These cells, which are quite closely arranged often in easily recognizable concentric layers, are usually designated from their form epithelioid cells. At the margin or outer limit of the nodule they are continuous with the cells of the surrounding tissue, but even under the microscope the outline of the tubercle is fairly distinct Among these cells, especially in the outer portion of the nodule, numbers of smaller cells are usually seen which are round and have relatively large, deeply staining round nuclei, cells which resemble very closely the lymphoid cells of the blood and are by most recent writers identified with those cells. These cells are supported by a network of reticulum of resistant fibrils which can be demonstrated by suitable methods. Similarly a network of fibrin filaments can usually be rendered visible throughout the nodule by the aid of the Weigert stain. Many tubercles show no further striking elements in their structures, but in the majority the well-known giant cells described by Langhans and Schuppel also occur. These are huge masses of protoplasm similar in general appearance to the epithelioid cells and often drawn out into long processes which ramify among the surrounding cells. They are provided with a large number of nuclei, often ten to twenty or more, which are usually arranged at the poles of the protoplasmic mass and often at its periphery in a ring so as to leave a central area devoid of nuclei and faintly granular.

Tubercle bacilli may usually be demonstrated by the staining method of Koch-Ziel-Nielsen and its modifications, lying among the epithelioid cells or in the protoplasm of these cells or of the giant cells. No vascular supply whatever can be seen in such nodules. Whatever vessels or capillaries existed at the point where the tubercle is formed become obliterated and disappear, and no new ones are formed among the new-formed cells. A colored injection of the vessels of an organ studded with tubercles, therefore,

leaves the tubercles as white nodules which stand out prominently on the deeply colored background of the rest of the tissue. This circumstance probably aids in bringing about the subsequent necrosis of the mass, although by itself it would not suffice to cause the death of such a minute nodule which might absorb sufficient nutriment from the surrounding fluids to maintain the life of the cells. Much more important in this respect is the action of the poison produced in the tissue by the bacilli, which first causes degenerative changes and finally the complete destruction of the cells. The nuclei of the epithelioid cells shrink and become twisted and distorted, and often so change their position as to lie with their long axis radially placed. For a time such nuclei take a very deep stain, but later they lose all power of taking up the stain. There appears among them, sometimes involving first the giant cell, but usually rather the adjacent portions of the tubercle, an area of complete disintegration of the tissue, the cells being converted into formless hyaline debris and caseous material.

Much discussion of the ultimate structure of the tubercle and of the origin of its elements has appeared recently in the literature. Fundamental work on this subject came from Baumgarten, but as to the earliest stages the more recent paper of Wechsberg seems of especial interest. He points out that in experimentally produced tubercles the initial change produced by the bacillus consists in an injury to the cells immediately about them as they lodge in the tissue. Following the destruction of tissue cells comes an inwandering of phagocytic leukocytes, which, however, are soon masked by the extraordinary proliferation of the fixed tissue elements of the connective-tissue nature, a proliferation analogous, it seems, to a healing process, but in this instance quite disproportionately intense when compared with the injury done to the tissues. Apparently there is a continuous injury or irritation which maintains the proliferation, and Baumgarten, indeed, holds that the primary effect of the tubercle bacillus is to cause the growth of tissue by the formative stimulus which it exerts.

As to the exact origin of the epithelioid cells opinions differ somewhat, some authors holding that they are derived from the endothelial cells of the vessels, while others regard them as arising from the neighboring connective-tissue cells or from epithelium, certain French authors even maintaining that they originate from wandering macrophages. It is now quite generally held that the lymphoid cells are phagocytic cells which have wandered into that position from the crevices of the tissue or from the blood stream, but there are those who still regard them as cells newly formed *in situ*. The giant cells seldom if ever show evidences of mitotic division in their nuclei, and doubt, therefore, still exists as to whether they are the product of the coalescence of several cells or of the continued division of the nucleus of a cell without the coincident division of the protoplasm. Baumgarten maintains that their presence is quite distinctive of tubercles as contrasted with miliary gummata, but the weight of evidence does not seem to favor this view, and it is probably impossible to distinguish between those two lesions merely upon their microscopic anatomical details.

As stated above, the tubercle nodules by no means always maintain their isolated character, but commonly become confluent or *conglomerated*, so that instead of forming rounded bodies the distribution is usually such that little groups or mulberry-like masses of tubercles arise. In these masses the concentric arrangement of the cells is often somewhat disturbed and irregular,

especially in the interior. Such confluent masses of tubercles may reach a considerable size, although usually not without undergoing the characteristic necrotic process, so that it is not uncommon to see in the spleen or elsewhere partly caseous tuberculous masses reaching a diameter of 1 cm. or more. Indeed, the so-called solitary tubercles are of a far greater size, sometimes even reaching a diameter of 4 or 5 cm. These are circumscribed masses of dense caseous matter surrounded by a capsule of distorted tubercles and tuberculous granulation tissue, which are apparently formed by the continued production and confluence of tubercles with degeneration and caseation of those more centrally placed. They appear most frequently in the brain, although usually associated with tuberculous lesions elsewhere in the body, and may constitute a tumor which by its bulk gives rise to disastrous consequences.

The common fate of the tubercle is caseation or necrosis of the more central portion. If sufficient time has elapsed perhaps the only exception to this is the conversion of certain small tubercles into a hyaline fibroid tissue, the fibroid tubercles mentioned above. The fact that a thin layer of living tuberculous tissue always remains about such caseous masses is probably due to the continuous extension and new formation of that tissue; nevertheless, it, too, is constantly encroached upon, leaving only ragged, distorted remnants of confluent tubercles.

The consistence of the caseous material varies in different cases, being sometimes very soft or semifluid, at other times firmer or of the consistence of cream cheese, while as time advances it may become dry and friable, or, when there is a deposit of lime salts, mortar-like. Further inspissation and the continued deposit of calcium leads with great frequency to the complete conversion of the caseous material into a stone-like substance, which is then practically an innocuous foreign body as far as the host is concerned. These changes, which tend toward the solidification of the caseous substance, indicate a diminution in the activity of the tubercle bacilli; the destructive process ceases to advance and the mass gradually becomes encapsulated by a growth of granulation tissue, just as in the case of any other foreign body. This encloses it completely and walls it off from the surrounding tissue, so that any remaining tubercle bacilli are imprisoned. Such encapsulated caseous nodules, sometimes as large as a cherry, are not uncommonly found in the lungs. The capsule is firm, hard, and deeply pigmented with coal and blood pigment, and the whole structure contracts until the nodule, even if it be not calcified, acquires a great degree of firmness. Anatomical evidence that a reinfection of the surrounding tissue may arise from such a nodule after it has become firmly encapsulated is very unsatisfactory, and in the cases of a renewed flaring up in an apparently healed focus, the new infection is probably not from any such healed lesion as just described, but rather from a still active though latent focus or from a new infection from outside.

The lodgement of tubercle bacilli in the tissues is not, however, always followed by the formation of definite tubercles alone. Frequently, especially on free surfaces, the formation of an abundant granulation tissue is associated with such tubercles. This tissue is highly vascular, and may be distinguished from ordinary granulation tissue not only by the presence of tubercles recognizable by their form and structure, but also by the abundance of epithelioid cells, identical with those which compose the tubercles, and which are scattered irregularly throughout Giant cells quite similar

to those seen in the tubercles may also be found. In such tissue there are even more definite evidences of the exudation of phagocytic cells from the bloodvessels than in the miliary tubercles themselves. Not only are there great numbers of lymphoid cells, but all those varieties of phagocytic cells which Maximow derives from the outwandered lymphoid cells are to be found in abundance. Particularly striking are the large irregular or rounded cells with large nucleus and very abundant protoplasm which are often most actively phagocytic, being found laden with fragments of cells and nuclear debris of all sorts. Typical plasma cells occur also in great profusion, and indeed it was in such tissue that Unna first recognized and described these cells. Polymorphonuclear leukocytes are not lacking and appear often in the most bizarre and distorted forms. The more superficial parts of the granulation tissue are usually somewhat œdematous and fibrin filaments can be demonstrated throughout. Such tissue, despite its rather rich vascular supply, contains tubercle bacilli and consequently undergoes the same necrotizing process as described for the miliary tubercle. Areas or foci of yellowish opacity appear below the surface of the pale grayish-pink, translucent granulations, and soon become confluent. In the same way the more superficial parts become opaque and yellow, and soon the whole becomes covered with a ragged grayish-yellow, pasty material, which is readily dislodged from the surface, and when the granulations form the lining of a sinus, constitutes, in part at least, the discharge. When formed upon a surface such as that of the pericardium and pleura the granulation tissue is usually covered with a thick, shaggy, yellow layer of fibrin, and is associated with an abundant exudate of fluid, which may be quite clear or turbid, with floating shreds of fibrin, or at times deeply blood-stained.

While the fresh granulation tissue in an active process shows the characters just described, there are tuberculous processes so slow in their development that there is time for the contraction and induration of the new tissue, and much of it escapes necrosis. The result is a scar-like tissue which may become extremely hard and firm and which may finally reach a considerable bulk. When this appears over the surface of the lungs or heart in the form of adhesions, binding the opposing surfaces together, it may by its rigidity and continued contraction cause great disturbances in the function of those organs. In the substance of organs such as the lung it may produce the densest and most widespread induration. The presence of such tissue in quantity is of course an indication of the very slow progression of the disease. Microscopically it is found to consist of an extremely compact fibrous tissue, in which no indication of its tuberculous nature may be found over large areas. Foci of plasma cells and lymphoid cells with scattered granules of blood pigment may occur. In other places, however, patches of caseation and groups of epithelioid cells or occasional giant cells may give indication as to its nature.

Other types of tuberculosis occur in which the lesion is for a time at least exclusively exudative in nature, *i. e.*, an acute inflammation. These are the instances in which the introduction of quantities of virulent bacilli into the tissues of a person of feeble resistance results in a destructive lesion which advances with extraordinary rapidity. Acute tuberculous inflammations are seen in their purest form in the lungs, but occur also in other places, such as the serous cavities and the meninges. The invasion of the bacilli, for example, into the lungs seems to produce an injury so intense that it is

responded to by a sudden pouring out of the elements of the blood almost exactly as in the case of the ordinary lobar or lobular pneumonia. The alveolar epithelial cells are desquamated and fall into the air cells, together with the abundant leukocytes and red corpuscles, which with the fibrin network and exuded fluid soon form a solid exudate very much like that in the simpler types of pneumonia. Characteristic of this sort of acute inflammation is its inevitable fate, which is necrosis or caseation involving not only the exudate but the included tissue. If the patient lives even a short time after the completion of this process, further proof of its tuberculous nature is given by the development of ordinary tubercles and tuberculous granulation tissue about the caseous area, and if life be further continued the picture may come to resemble closely or precisely that produced in the other ways described.

The intimate relation which exists between these forms of tuberculous lesion may be readily seen. Since the demonstration of the tubercle bacillus by Koch there can be no further question as to the unity of the process, although Orth still seeks to maintain a duality on anatomical grounds. It is plain that although bacteria which are secondary invaders may occasionally appear, the tubercle bacillus is the essential cause of all the changes. Further, even on anatomical grounds there is no very sharp line which we can draw between them. The acute inflammatory form involves the most rapid reaction on the part of the vessels and wandering cells, and it is only in the later stages that proliferative processes occur, although finally they also occur. In the miliary tubercles, as Wechsberg has shown, we have also a primary injury, a response on the part of the leukocytes, which, however, is soon masked by the excessive reaction among the fixed cells. The fact, however, that if sufficient time elapses there are almost invariably traces of the formation of tubercles and the analogous tuberculous granulation tissue in the margins of the areas of acute inflammation shows clearly enough that these are varieties of the same process. The differences in the anatomical result seem to be due to a number of circumstances, among which perhaps the specific power of resistance of the individual is most important. In certain persons the bacilli meet with unfavorable conditions for growth, so that probably in the majority of those into whose tissues they pass they are almost at once destroyed by the phagocytic cells or at most produce only a small local lesion which is soon completely encapsulated and healed. In others, however, they spread like fire in flax, destroying the tissues with frightful rapidity. Further, the virulence of the particular organisms introduced and their number are of great importance in determining the type of lesion, for while small numbers of bacilli inhaled into the respiratory tract may be fairly well restrained in their growth for a time, they may multiply slowly in the tissue, gradually gaining power to overcome the destructive influence of the protective agents of the body. Such a focus of "acclimated" tubercle bacilli may appear, for example, as a caseous area in a bronchial lymph gland: then if the adjacent bronchial wall be eroded through by the advancing necrosis, great quantities of highly virulent bacilli are suddenly discharged into the bronchus and further into the lung, usually causing the so-called *phthisis florida* or *galloping consumption*. In this case, although the changes in the bronchial lymph gland are found to consist of conglomerated and caseous tubercles, those in the lung have the type of an acute exudative inflammation.

Again, the exact mode of the introduction of the bacilli and the anatomical character of the tissue in which they find lodgement are important. Thus, if such a caseous gland erodes the wall of a vein and discharges its infected contents into the blood stream, the common result is the simultaneous appearance of miliary tubercles thickly sown throughout all the organs of the body, and while these are perfectly typical in such organs as the liver and spleen they often partake more largely of the nature of minute bronchopneumonic patches in the lungs.

There is in common among these varieties of anatomical lesions the tendency to coagulative necrosis or caseation, with the consequent destruction not only of the exudate or newly formed tissue cells, but also of the tissue within which this process takes place. The injury produced by the tubercle bacillus to the tissues, while so slight at first as to have been long overlooked in the general interest aroused by the proliferative reaction, is continuous and finally leads to the destruction of all of the new-formed tissue as well as the included structures. The spread of the tuberculous process and the consequent destruction of tissue are limited in greater or less degree by the erection of a resistant barrier of scar tissue by the surrounding structures, which may in time accomplish the complete healing or cicatrization of the lesion. In fact, one may discover, in nearly every autopsy upon the body of persons in advanced life, the pigmented scars of such healed tuberculous lesions. These are, it is true, usually quite small, and show that the lesion was never an advanced one; but in some instances quite extensive tuberculous infections are found to have been overcome, and even a relatively large cavern in the lung may be cleaned out and be converted into a smooth-walled cavity which is finally relined by epithelium. Indeed, the frequency of such healed lesions in the bodies of those who have reached adult life is astounding, as may be gathered from Naegeli's statistics, in which, in the examination of 500 cases at autopsy, recognizable tuberculous lesions were found in 98 per cent. The significance of this in showing the ability of the human body to resist the inroads of the bacilli is very important.

In addition to the actual destruction of tissue, certain general results of the existence of tuberculosis in the body become apparent. Great emaciation of the whole body usually accompanies the disease, although in exceptional cases extreme obesity persists. In the later stages the emaciation is associated with a peculiar cachexia which is very characteristic. With this, anæmia of a secondary type may become extreme. In the internal organs the effect of the toxins is often to cause epithelial degenerations, so that it is not uncommon to find profound fatty metamorphosis of the liver and kidneys, doubtless partly due also to the anæmia. Indeed, one sometimes finds in a tuberculous case in which the emaciation has proceeded to the greatest extreme, the liver weighing far more than normal and loaded with fat.

**Modes of Entry and Distribution of the Bacilli.**—The conditions of existence of the tubercle bacilli outside the body are sufficiently well known to explain fairly well the mode of its entrance into the body, although of late much spirited discussion has arisen as to the relative frequency of these different modes of entry.

Of these the inhalation of the bacilli into the lungs or at least into their large air passages has long been regarded as the most important. Until recently, too, it was generally thought that the most favorable conditions

for this are those in which the bacillus is perfectly dry, and mingled with the dust of dried sputum, etc., is blown about in the air and thus directly breathed in. The work of Flügge and his pupils, however, seems to show that an equal if not greater danger exists in the respiration of air immediately about consumptives, who have been shown to send off in breathing and talking, but especially in coughing, sneezing, laughing, etc., a fine spray of minute droplets, many of which are laden with tubercle bacilli. Such a cloud of spray may extend for a distance of at least four feet from the patient's face and be breathed in by anyone within that radius. This idea has been repeatedly confirmed by the microscopic study of slides exposed before the face of such a patient and by experiments with susceptible animals similarly exposed.

The bacilli may enter the nose and mouth, and are in large part like other dust received by the cilia of the upper respiratory tract and wafted back harmless. Others, however, gain lodgement, and it is as to the point of their primary lodgement that so much dispute has arisen.

Two probabilities are prominent: either the bacilli which escape the action of the cilia may reach the smaller bronchi or the tissues of the lung, or they may pass into the walls of the air passages. In the latter case they are usually transported to the neighboring mass of lymphoid tissue. In both instances they may immediately produce a local lesion or pass into the tissues precisely as coal-dust or any other fine, innocuous particles, and be carried by the lymphatic channels to the lymph glands which drain that area, where they then lodge and produce the characteristic lesion. These initial lesions will be described in dealing with tuberculosis of the respiratory tract, and it may merely be said here that in the invasion of the upper air passages it is chiefly the superficial lymphoid tissue which is so abundant in the pharynx (tonsils, Luschka's tonsil, numerous scattered lymphoid nodules, etc.) which is thought to become the channel of entry of the bacilli or in other more fortunate cases the means of their destruction.

Great differences of opinion have prevailed as to the importance of those lymphoid structures of the pharynx and the cervical lymph glands in the production of tuberculosis of the lungs. While Grober claims that infection of the cervical chain may conduct the bacilli directly to the dome of the pleura and thence to the lungs, and others state that infection of the bronchial glands may be brought about in a similiar way, Beitzke in a recent paper shows by careful injection that particles can be transferred from the cervical glands to the lungs only by way of the main lymphatic trunk, the right heart, and the pulmonary artery.

Renewed attention has recently been directed to infection by ingestion of food containing tubercle bacilli, by the writings of v. Behring, who holds that perhaps a majority of the cases of tuberculosis in young people are the result of the introduction of tubercle bacilli through the intestinal wall from infected milk. This infection takes place at a very early age, the bacilli remaining latent or dormant until much later, when, on the advent of a condition of lowered resistance, they begin to grow and destroy the tissues. Klebs had previously enunciated the possibility that pulmonary tuberculosis might result from an intestinal infection without necessarily being associated with any extensive tuberculosis of the intestine, and the frequent occurrence of widespread tuberculosis of the mesenteric glands in children seems to add weight to the theory. It is difficult, however, to con-

vince one's self that this plays a prominent part in the inception of tuberculosis in more advanced life, and it seems more plausible to regard the intestinal ulcers so frequently found in those cases as entirely secondary and due to the swallowing of tubercle bacilli in the sputum from the diseased lungs. Nevertheless, the enormous danger to children in the ingestion of milk containing the bacilli must not be underestimated. The recent work of Ravenel and others in feeding tubercle bacilli in butter to animals, with the demonstration of bacilli in the mesentery, although no actual lesions of the intestinal mucosa are produced, is important.

We are less well informed as to infections through the skin or by way of wounds. There are various tuberculous affections of the skin, such as lupus, which are probably due to direct infection. Actual tuberculous ulcers may also occur. The infection of wounds with the tubercle bacilli is not a very common cause of generalized tuberculosis. The so-called necrogenic tubercles are not usually productive of general tuberculosis, although in certain instances they have been followed by the disease. Nor is it usual to find any extensive distribution of tubercles from infected wounds, although in at least one instance recently seen a definite tuberculosis of the epitrochlear gland occurred consequent upon a tuberculous infection of the finger of a student who had performed an autopsy on a tuberculous patient.

Tuberculous infection of the genital tract by means of coitus with a person suffering in a similar way may occur, but cannot be regarded as common, and most of the cases of genital tuberculosis, both in males and females, are with more justice considered to be due to a spread of the process from other and perhaps concealed foci. Baumgarten, however, described the infection of the epididymis along the vas deferens and, further, the experimental production of tuberculosis of the lungs by the introduction of tubercle bacilli into the urinary bladder.

After the admission of the active bacilli into the body there are certain conditions which govern their localization and growth. Of these the mechanical means of distribution are very important, but certain tissues offer more favorable soil for the growth of the organisms than others. Thus, for reasons with which we are not acquainted, the apical portions of the lungs are particularly prone to such lesions. So also are the adrenal glands and the epididymis, while tuberculosis of the lower part of the lungs ordinarily appears only later and secondarily, and tuberculosis of the testicle almost regularly only as a result of tuberculosis of the epididymis. Even more important and interesting are the points of least resistance which may be constituted temporarily by some injury of the tissue or disturbance of its nutrition. Good examples of this are described by surgeons in the development of tuberculosis of bones or joints after their injury by fall or strain.

The mechanical distribution of the bacilli is effected in several ways, depending largely upon their mode of entry. Of these one of the most common is that in which the bacilli are carried along the lymphatic channel until they lodge in the vessels of the sinuses of the lymph glands which form stations in those channels. In their course along these channels many of them adhere to the endothelial walls and there produce tuberculous lesions which may be readily visible as grayish or yellowish nodules, and where, as in the case of the mesenteric lymphatics, an opaque lymph is ordinarily

carried; these become very conspicuous by their distention with chylous fluid which can only with difficulty pass the obstructing tubercles.

Thus we find the peribronchial lymph glands regularly involved in a tuberculous, caseating process when there is tuberculosis of the lung, the mediastinal and retroperitoneal glands in cases of tuberculous peritonitis, mesenteric glands in intestinal tuberculosis, and so on. Nor is it always easy to explain the distribution on the supposed direction of the lymph stream, for there are sometimes found to be glands diseased which do not seem to be in the line of flow toward the centre, and this has given rise to the idea of a retrograde transport, *i. e.*, the passage, whether by obstruction or reversal of the stream or by growth and extension of the bacilli, toward glands which are situated in a position which ordinarily drains *into* the affected area and not out of it. The distribution in the lymphatic system is thus seen to correspond closely with that of any foreign particles which get into the tissues or with the cells of an invading carcinoma. In certain cases even the thoracic duct becomes the seat of mural tuberculous lesions which may cause partial obstruction, but which allow of so extensive sifting of tubercle bacilli into the blood stream as to give rise to a generalized acute miliary tuberculosis.

This is one common mode of wholesale introduction of bacilli into the blood stream, but another method exists, namely, the rupture of a caseous gland directly into a vein. The wall of the vein becomes involved in the tuberculous process from without, and as caseation advances it slowly eats through the wall until finally a friable plug of yellow material loaded with bacilli projects into the blood stream, or the semifluid caseous material is actually washed out of the gland into the vein. This, again, is almost always followed by a widespread miliary tuberculosis.

Similarly, the great serous cavities may become infected by the rupture into them of adjacent caseous lymph glands or by direct extension from a tuberculous lesion immediately underlying the wall of such a cavity, as, for example, a tuberculous ulcer of the intestine. Direct extension of the lesion is perhaps better exemplified in the so-called ascending genito-urinary tuberculosis in which, one after another, epididymis, vas deferens, seminal vesicles, prostate, bladder, ureters, and pelvis of the kidney are affected, although whether the extension occurs in this order or not has been the subject of recent discussion.

In a very similar way tubercle bacilli may be transported from one part of the intestinal tract to another, giving rise to ulcerative lesions as they go, and from one part of the lung to another along the bronchi by the aid of the respiratory currents of air and gravity.

**Acute Miliary Tuberculosis.**—It is not easy to draw a sharp line between generalized and acute miliary tuberculosis and the occurrence of scattered tubercles of various ages in the organs in association with tuberculous disease of longer standing. The type, however, of acute miliary tuberculosis as generally recognized is that condition in which with high fever and a stuporous intoxication resembling that of typhoid fever there is found at autopsy a general distribution of minute tubercles, all of practically the same age and size throughout almost all of the tissues. In such a case we may presume that the bacilli reached the tissues at about the same time and therefore that they must have been conveyed by the blood stream. The same is true of those tubercles which are scattered in numbers in the organ, but

which vary greatly in age and size, except that in that case the bacilli apparently gain access to the blood stream a few at a time, and possibly not at all in the sudden wholesale way which may be demonstrated in the typical generalized miliary tuberculosis. In those typical cases it has become more and more evident since Weigert's publications on the subject, that if sufficient search be made an intravascular tubercle directly distributing bacilli into the blood stream or an ulcerative tuberculous lesion of the thoracic duct may be found. The percentage of positive results in the search for vascular tubercles in cases of miliary tuberculosis is very high (70.8 per cent. in Weigert's cases, 82.8 per cent. in Sigg's, and over 90 per cent. in Schmorl's cases).

The tissues contain a very great number of nodules, not billions, however, but thousands, as Cornet points out, and still if one remember the small size of the bacilli, it will be seen that enough bacilli to produce so many nodules may be easily furnished by a small quantity of caseous material rich in organisms. Tuberculous lesions of the vessels which involve the direct exposure of caseous bacillus-holding material to the blood stream are found most commonly in the pulmonary veins, although they also have been found repeatedly in the vena cava superior and less often in the azygos, adrenal, jugular, and cerebral veins. Careful examination of these lesions shows that they fall into two groups which, as pointed out by Benda in his recent admirable review (Lubarsch and Ostertag's *Ergebnisse*), are the result of different processes. In the one instance a tuberculous process approaching the vessel from without erodes its outer wall, and may in time perforate it, either causing thrombosis or by its more sudden advance entering the vessel before it has time to be obliterated and discharging the caseous material with bacilli into the passing blood stream. This is the so-called periangeitis caseosa.

On the other hand, the tuberculous lesion may be limited to the intima of the vessel and evidently produced by the deposition of floating tubercle bacilli from the blood stream upon it. Such lesions may occur in the endocardium or in the intima of the aorta or even of the smaller arteries, but are more common in the veins. In a recent case in which such a caseous mass was found in a pulmonary venule, the lumen of the venule was completely filled so that no blood passed, and it would have had no significance in the further distribution of bacilli had it not grown to project free into the larger vein into which the branch emptied. From this free end there was sufficient distribution of bacteria to produce tubercles in all the organs. The free surfaces of this projection were perfectly smooth and rounded, but, as Benda points out, it is quite possible that enough material had been broken off from this projection to produce tubercles everywhere, and that then the deposit of fibrin and the constant passage of the blood stream smoothed over the end of the caseous mass. In a study of these cases Whipple has been able to ascertain the existence of tubercles formed in the walls of large bloodvessels evidently by the entrance of the bacilli into the vasa vasorum. He has further observed that in the case of intimal tubercles the caseous material is rarely found to be directly exposed to the circulating blood, but is rapidly covered with a thrombus over which the endothelium may grow with great rapidity, thus temporarily preventing the further discharge of bacilli. This renders it probable that these vascular tubercles may after all deliver their tubercle bacilli to the blood, in instalments, as it

were, and thus produce several crops of tubercles often differing but little in age.

Finally, tuberculosis of the thoracic duct may be the result of the invasion from neighboring tissues, but apparently more often follows the distribution of bacilli upon its intima or the extension of caseous thrombi of its branches into it. It may affect only one area, or almost the whole length of the duct may be involved with occlusion here and there and ulceration of the masses which line it. Stasis of lymph and the development of collateral circulation are generally evident. Such a duct will of course pour quantities of bacilli into the subclavian veins and thus into the right heart and pulmonary circulation. It seems important also that cases occur in which no lesion of the thoracic duct is to be made out, but in which, nevertheless, abundant tubercle bacilli are demonstrable in the contents of the duct, probably swept into it from caseous abdominal lymph glands. Several such cases have recently come to the writer's notice, and it seems quite possible that in this way alone there might arise a wide distribution of tubercles.

It is important to remember that tubercle bacilli are extremely small, and can readily pass where a red corpuscle can pass. There is, therefore, no reason why they should not pass through the lungs from a systemic vein and be deposited in some other organ. Still, it has been shown that they are very quickly removed from the blood and do not circulate long nor increase in number in the moving blood. Thus it is that the lungs, forming as they do the first sieve for the blood, usually show the tubercles in a more advanced stage than elsewhere, while in the case of invasion of the portal vein the liver may be the first organ to develop tubercles.

In reaching the tissues the bacilli may immediately produce lesions at the point of deposition or be transported as innocuous foreign particles for a small distance into the tissues and there set up destructive changes. Thus in the acute miliary tuberculosis of the lungs it is not uncommon to find, on closer examination of the nodules, that instead of centring as nodules about the capillary vessels they are really minute areas of tuberculous pneumonia.

But little need be said further in regard to the pathological anatomy of the condition. Usually, there are older caseous foci of tuberculosis to which the development of the vascular lesion may be traced and the acute miliary tuberculosis is then in a way the terminal event of a chronic tuberculosis. Why symptoms of such profound intoxication should arise in these cases is not quite clear, for there are many other conditions which do not show any such intense symptoms, in which there is quite as much or far more tuberculous tissue and as many or more tubercle bacilli growing in the tissue.

According to the duration of life of the host after the distribution of the bacilli the tubercles, which are scattered everywhere, may vary from minute translucent grains to larger nodules with a central point of beginning caseation. There may be a difference in the size of the nodules in the lungs and in the other organs, but very often this does not appear. No organ seems exempt. Serous surfaces, bone-marrow, retina, myocardium, thyroid, etc., may show miliary tubercles. Little mention is made of them, however, in the muscle and skin.

**Tuberculosis of the Respiratory System.—Nose.**—The mucosa of the nose is probably more often the seat of tuberculous lesions than is generally

supposed. It may be infected from soiled handkerchiefs or fingers, from the passage of tuberculous sputum when the lungs are affected, or perhaps by the direct inhalation of tubercle bacilli. Experimentally it has been shown that tuberculosis of the nasal mucosa of guinea-pigs may be produced without any wound of the mucosa by spraying tubercle bacilli into the nostril. Further, it has been shown that in normal individuals tubercle bacilli may sometimes be demonstrated in the nasal secretion. The lesions, according to Herzog and others, may be ulcerative upon an infiltrated base, they may form circumscribed tumors, or they may consist in a combination of these types. They affect most often the vault of the nasal cavity where it passes over into the pharynx, the septum, and the inferior turbinate. The accessory sinuses, however, may be involved and caries of the sphenoid and other adjacent bony structures has been reported. In certain cases, as is true also of the mouth, pharynx, and even of the larynx, the lesions of lupus, with their shallow ulcerations and subsequent scarring, may extend from the skin into the nasal cavity.

**Larynx.**—The tuberculous alterations of the larynx are in principle similar to those of the nasal cavity. They are common in association with pulmonary tuberculosis, but occur also as a primary affection. There seems little doubt that when the larynx shows tuberculous ulcerations co-existing with a tuberculous cavity in the lung, the laryngeal tuberculosis is secondary and due to infection of the larynx by the passage of the sputum. There are those, however, who hold that it is of hæmatogenous origin and in certain cases in which miliary tubercles are found in the mucosa alone this may be correct. The evidence in favor of the direct infection by sputum is overwhelmingly strong, and even when the lesions in the larynx are more extensive than those in the lung it remains possible to explain the fact on the ground that the pulmonary lesions have ceased to advance so rapidly as those in the larynx.

Tubercles appear in the mucosa as minute gray nodules, usually under the epithelium. Evidently the bacilli may be absorbed between the epithelial cells as foreign bodies and produce a lesion only after reaching the underlying tissues. The coalescence, extension, and subsequent caseation of such tubercles results in the formation of ulcers. These may be small, rounded, shallow losses of substance, sometimes edged with a yellow, opaque line, and showing a reddened base, or they may be large, ragged, irregular, and deep ulcerations. The first or aphthous erosions may occupy a large part of the lining mucosa and are especially often found to extend in great numbers along the course of the trachea. The more extensive ulcerations affect most commonly the true and false vocal cords, the arytenoid cartilages and the epiglottis, but may of course involve any part or all of the larynx, or even extend to the adjacent pharynx and trachea. Like similar ulcers elsewhere, they are irregular in outline, sometimes very precipitous with ragged margins and reddened base, often showing gray or yellow, opaque nodules and a lining of shreddy material or a considerable caseous and purulent secretion. They may extend deep into the tissues, and cause great destruction of the vocal cords, the edges of which are so excavated as to be incapable of performing their function. The laryngeal walls in general are often deeply eroded and the destructive effects may be especially disastrous in the case of the epiglottis, which may be completely destroyed so that swallowing becomes very difficult. The tuberculous perichondritis, which is part of this process,

by destroying the perichondrium, causes necrosis of the cartilages, which finally become denuded and often deeply eroded. Sometimes in the course of such a destructive ulcerative process a secondary infection may occur, producing a phlegmonous or gangrenous laryngitis, often with a rapidly fatal result.

Lupus-like proliferative forms of tuberculosis occur in the larynx and may be direct extensions from similar lesions in the pharynx. They produce flattened elevations and shallow ulcerations and subsequently extensive scars. Recently, Panzer and others have pointed out that papillary excrescences formerly regarded as papillomatous in nature may in many cases be tuberculous. These are often pedunculated or sessile, cauliflower-like structures which are bluish in color and ragged or uneven superficially, and are largely composed of tubercles and tuberculous granulation tissue. Cases of healing of tuberculous ulceration of the larynx are extremely rare; partial healing may of course frequently occur and cicatrization may in some instances be extensive enough to produce stenosis of the larynx.

**Trachea.**—In the trachea the shallow, aphthous ulcers form the common type of the tuberculous lesion, and may be found closely set throughout the whole mucosa or scattered singly here and there. Frequently such tuberculous lesions of the larynx and trachea are associated with caseous foci in the immediately adjacent lymph glands which may become adherent. Indeed, as in a case recently seen at autopsy, sinuses may form, connecting the lymph glands with the perforated ulcers in the trachea, and the extension of the process may lead to the complete isolation of the trachea which comes to lie in a sort of sheath lined with tuberculous granulation tissue and oozing, caseous fluid matter. The question might well arise in such a case as to whether the focus in the lymph glands outside the trachea was not the primary one, the ulceration of the tracheal mucosa being due to their rupture into its lumen.

**Bronchi.**—Tuberculous lesions of the bronchi are practically invariably associated with tuberculosis of the lungs and may be described with that condition.

**Tuberculosis of the Lungs.**—The pathological anatomy of tuberculous diseases of the lungs presents a remarkably varied picture, the changes differing greatly in character according to the intensity of the affection and the consequent duration of the disease. These variations depend upon the number and virulence of the bacilli and their mode of introduction, and, on the other hand, upon the resistance of the individual.

Under ordinary circumstances the disease begins in the apical portion of the lung, not quite at the apex, but usually at a point about 2 cm. below the extreme apex, and there the primary lesion usually takes the form of a small, caseous focus involving the termination of the small bronchus which extends to that point. Indeed, Birch-Hirschfeld insists that the mode of formation of the initial lesions consists essentially in the primary localization of the inhaled bacilli in the terminal portion of the bronchus just as it passes over into the atrium and in the formation there of a caseous and ulcerative bronchiolitis which soon extends to involve the adjacent air cells and the neighboring bronchial wall. This simple explanation is not agreed on by all, Ribbert thinking the apical lesion to be most frequently the result of the secondary introduction of the bacilli into the lung after they have already passed through it and been transported to the bronchial lymph glands as any innocuous particles of dust, being again set free into the

[illegible]

of the lung. Usually the extension is at first quite local and leads merely to the enlargement of the focus with the involvement of the surrounding pulmonary tissue. This may proceed by the rapid appearance of a group of small conglomerated tubercles which occupy the air cells, to the exclusion of the air, and soon associate with themselves so much cellular exudate and tuberculous granulation tissue as to render that area quite solid. The caseation soon extends from the central bronchus to involve all the central part of this solid tissue, including in the necrosis the walls of the air cells, bloodvessels, and all that was formerly the lung tissue. With the advance of the necrosis the bloodvessels become completely obliterated so that when the caseous material is finally liquefied and discharged into the central bronchus, whose walls were the first to be destroyed, no hemorrhage takes place. In such early lesions the discharge of the caseous matter into the bronchus is practically always possible on account of the inevitable wide connection of the bronchus with the cavity or vomica thus formed, and one can at autopsy almost invariably pass a probe from any tuberculous cavity directly into a bronchus. The cavity thus formed may be very small and no larger than a marble, but the emptying of its contents into a bronchus is usually the first step in the wide involvement of the lung in the tuberculous process. The presence of the material, loaded as it is with tubercle bacilli, in the larger bronchi provokes violent respiratory movements and cough, and these aided by gravity soon effect the distribution of the bacilli back into the previously uninfected bronchi.

When the aspirated substance reaches the finest bronchioles and the associated air-containing tissue, tuberculous lesions quickly result, and these again vary somewhat in character according to the virulence and number of the bacilli and the consequent rapidity and extent of the change. Apparently they are ordinarily of pneumonic or exudative character in the earliest stages, but when they come to view at autopsy they have usually had time to undergo a partial caseation, together with the marginal development of irregular conglomerated tubercles which add to the firmness of each patch and render them indistinguishable from partly caseous conglomerated tubercles, except by the fact that the microscope reveals the framework of the air cells undisturbed in its relations, which is outlined throughout the caseous area by the elastic tissue which persists for a long time. This seems characteristic of a pneumonic area, for the primary development of conglomerated tubercles in the air-containing tissue leads to the great displacement of the walls of the air cells and their great distortion before they have time to undergo caseation. Nevertheless, it is by no means uncommon in such cases to find abundant miliary and conglomerate tubercles scattered throughout the lung as the result of the aspiration of infected material. If the anatomical study of the lung can be carried out soon enough after the aspiration of the bacilli it is easy to distinguish microscopically between the minute areas of pneumonia and any definite fresh tubercles which may occur. Still, as described, the exudative processes, the proliferative process, and the process of necrosis are so quickly combined that in principle a fairly uniform result ensues. The gross appearance of such a lung may, however, vary greatly. It is most common on section to find the lung moist, but not particularly hyperæmic and studded throughout with firm patches of various sizes which are usually ranged around the bronchi like clusters of grapes about the stem. These consolidated patches, when very small, may be

pearly gray and semitranslucent, and most easily recognized by the palpating finger, but when large they present a flat surface elevated a little above the cut surface of the lung and roughened and opaque or dull in appearance. In color, they alter with age from a grayish red, through gray to a pale yellowish white. With the further lapse of time they undergo softening and liquefaction and a greenish hue may become apparent in the caseous material. About them the lung substance is usually moist and reddened or grayish in color. It is more translucent than normal and exudes on pressure a tenacious, glutinous fluid. In other instances the patches are much firmer and project mulberry-like above the cut surface, giving it a very nodular appearance.

Such is the ordinary appearance of the tuberculous lobular pneumonia or bronchopneumonia which results from aspiration of the contents of the primary apical cavity, and this may be regarded as by far the commonest type of pulmonary tuberculosis. Associated lesions of the pleura, lymphatic system, etc., always occur, but these may be described separately.

No fundamental distinction can be made between this type of pulmonary disease and that which was so clearly described by Fränkel and Troje under the name of acute pneumonic phthisis. In that condition the sudden introduction of large numbers of virulent tubercle bacilli into the bronchi results in the rapid appearance of a widespread consolidation of a whole lobe or even of the whole lung, so that the condition is often regarded as ordinary acute lobar pneumonia. In no essential point, except in degree of involvement and rapidity of development, does this alteration differ from that just described in the acute lobular bronchopneumonia. The appearance of the lung is, however, very characteristic, especially in the more advanced stages. At first the consolidated area has practically the appearance of that seen in acute lobar pneumonia. The whole lobe is evenly consolidated, its pleural surface being dulled by an opaque deposit of fibrin. The cut surface is roughened by minute fibrinous plugs, and the whole opaque, dull-looking area has a grayish or grayish-red color. The adjacent lung not actually involved in the definite consolidation has the gelatinous semitranslucent appearance described also for the lobular pneumonia, and if one stroke it with a knife it is sometimes possible to draw up into strings the gelatinous fluid which exudes from it. It is rare, however, that the lung in this condition shows only these appearances; ordinarily some part or all of the consolidated area has undergone the inevitable caseation or coagulative necrosis so characteristic of tuberculous lesions. Usually, this is irregularly distributed so that the cut surface has a marbled appearance, but sometimes, as in a recent case at the Johns Hopkins Hospital, the whole lung is quite uniformly converted into a homogeneous, yellowish-white material which cuts smoothly like cream cheese and shows no living tissue with the exception of the largest vessels and bronchi. In this case the small cavity in the apical portion of the lung showed clearly the mode of distribution of the infectious agent. If an attempt be made to inject such tuberculous lungs, it is found that the injection mass stops short at the margins of the necrotic areas, although the capillaries are still quite patent in the gelatinous areas and in the fresher portions of the pneumonic consolidation. It results from this that in such a case as that described, in which the whole substance of the lung had undergone caseation, the colored mass would enter only the larger vessels.

Microscopically, the development of these lesions is about as follows: Under certain circumstances the bacilli may spread along the lymphatics

or for a short distance through the tissue and set up the formation of miliary and conglomerated tubercles of the usual type. As will be described, such tubercles may develop throughout the lung when the bacilli enter by the blood stream.

As to the earliest stages in the formation of the more usual or pneumonic lesions we are able to judge as in ordinary pneumonia, chiefly from the appearances of the changes in the neighborhood of the more advanced lesions. There we find bloodvessels distended with blood and the air cells filled no longer with air, but with a fluid the viscidity of which is indicated by the deep eosin stain which it takes in the section. Many large cells with round, vesicular nuclei and abundant protoplasm, often studded with fat globules, lie in this fluid, and are for the most part to be regarded as the desquamated alveolar epithelium from the walls of the air cells.

Mononuclear leukocytes of various sizes, a few red corpuscles, and increasingly abundant polymorphonuclear leukocytes are soon associated with these. A dense network of fibrin is not long in forming, and finally, except for the great abundance of desquamated epithelial cells, the appearance is not unlike that of ordinary pneumonia.

Scarcely, however, is the exudate completely formed when the change occurs which is particularly characteristic and which will serve at once to distinguish tuberculous pneumonia from the ordinary forms. This is the process of coagulative necrosis which changes the cellular exudate into the red staining, formless material, in which at first abundant deeply staining fragments of nuclei are visible. They are seen as fine dust-like particles in clouds about the margin of the caseous area, where they are conspicuous by their deep blue stain. Elsewhere the whole area is converted into a fairly homogeneous refractile granular pink or red staining substance. In time the caseous material becomes more and more homogeneous although at first shadowy outlines of the cells of the exudate are distinguishable. The walls of the air cells which are also involved in the necrosis fade away gradually and are finally lost in the softening debris. As long, however, as the caseous material retains its firm consistency these walls can be distinguished usually as faint lines of pale blue. By the aid of Weigert's special stain for elastic tissue they may be plainly brought to view as a network of deeply staining fibrils, for it is chiefly owing to the great abundance and great powers of resistance of the elastic tissue that they remain visible so long. Even after the caseous area becomes liquefied and is expectorated through the bronchi, shreds of elastic tissue persist and may be recognized in the sputum. The presence of the elastic tissue, in the normal architectural arrangement without distortion, throughout the caseous area, gives proof, as mentioned, of the pneumonic origin of the lesion rather than its dependence upon the formation and subsequent caseation of tubercles. Certain other structures persist within the caseous areas and may remain recognizable for a long time. Particularly resistant are the larger bloodvessels the walls of which become extraordinarily thickened on the stimulus of the advancing destructive process. The thickening is especially seen in the inner layers, which become so increased in bulk as to obliterate the lumen of the vessel—the so-called obliterative endarteritis. Coal pigment in the walls of these vessels is an aid in their recognition. The bronchi which are included are also often distinguishable by the presence of coal pigment in their walls, but they show far less power of resistance than the

bloodvessels. Indeed, their walls are quite commonly involved in the caseous process throughout considerable lengths. In some instances the bronchi are rendered conspicuous by the great thickening and subsequent caseation of their walls, even when they are not completely surrounded by caseous material, so that they run as thick-walled tubes of opaque, yellow material through the gelatinous or partly consolidated lung.

Even when the caseation is apparently quite homogeneous over an area of the lung, it is often seen on microscopic examination that there are in the firmer caseous substance rounded and irregular cavities which contain a loose network of coarse fibrin filaments, often with scarcely any cellular remains. These are often at the terminations of the small bronchioles, where they pass over into the vestibule and atria; in many cases they are surrounded by the remains of the walls of normally disposed air cells and have not been produced by the breaking of one air cell into another. The most plausible explanation of their presence seems to be that the solid caseous material once formed may be in small part discharged through the bronchus or it may contract in such a way as to leave cavities such as are seen in a Swiss cheese. The coagulation of new fluid which permeates into their cavities results in the coarse, loose networks of fibrin described.

Up to this point, then, we have larger or smaller areas of pneumonic consolidation in which the greater portion is completely necrotic, although still showing indistinctly the architecture of the tissue, while the marginal portion, although still living, is densely infiltrated with the cells of the exudate fluid and fibrin. Such areas are surrounded by wide halos of the gelatinous infiltration in which the air cells are filled with fluid and desquamated epithelial cells. This is the so-called *caseous* and *gelatinous pneumonia.*

The further outcome of this condition varies considerably. Actual resolution is probably unusual if not entirely impossible when the consolidation is completed. In the areas of collateral œdema or gelatinous pneumonia which surround the patches of consolidation it seems probable that the exudate may disappear in case the actually caseated area becomes limited and encapsulated. This must be chiefly a mechanical process, for any such general autolysis and dissolution of the exudate as occurs in lobar pneumonia of the ordinary type seems to take place only in the slightest degree, if at all, in tuberculosis. Further, the obliteration of the bloodvessels which is practically never observed in the ordinary pneumonia, takes place very early in the tuberculous process, and that area is then completely cut off from any hope of favorable influence from without.

When the caseation is complete it is usually found, in those cases in which the patient has lived at least a short time after the death of the tissue, that organization of the exudate which has not become necrotic occurs. This accordingly affects the contents of the alveoli around the margins of the caseous area and is a process in every way analogous to that seen in ordinary pneumonia, in the margins of the necrotizing areas in glanders of the lung, in actinomycosis, etc. Ordinarily the organization as it appears a little distance from the caseous area is non-specific in character and not to be distinguished from that seen in any bronchopneumonia. Within this, however, and immediately adjacent to the caseous area, abortive irregular tubercles and dense tuberculous granulation tissue develop in which giant cells are frequent and epithelioid cells form the predominant element. These processes together form a fairly dense fibrous wall about the caseous mass,

a wall which is, however, prone to further necrosis and disintegration. The walls of the air cells and vessels, which in this type of pneumonia become especially intensely infiltrated with the cellular exudate, are included and built up into this capsule.

Sometimes such an encapsulation is effective in limiting the further action of the tubercle bacilli upon the tissues, the caseous material is retained by it and becomes denser and dryer, until finally with the deposition of calcium salts it may practically be converted into a stony or mortar-like substance. Usually, however, a quite different result ensues. The caseous material becomes softened and finally liquefied or broken down into a mushy, thick fluid which is discharged into the open bronchus and when mingled with the mucous secretion of the bronchus forms the green sputum which, according to Fränkel and Troje, is so characteristic of the acute caseous pneumonia.

The discharge of this material leaves a cavity which, when all the caseated tissue is liquefied and expectorated, corresponds in form and size with the focus of pneumonia. In some cases, in which the caseation advances with great rapidity and quickly involves large areas of the lung, the cavity formation may also be extremely rapid and extensive so as to practically completely destroy the lung within a very short time—the so-called *phthisis florida*. The wall of such a cavity consists of a more or less dense membrane-like layer of tissue, the lining of which is composed of necrotic, shreddy material which remains after the discharge of most of the caseous area. Beneath this is the tuberculous granulation tissue which is essentially the same, no matter where formed. Even outside of this in the earlier stages there is the lung tissue partly consolidated by cellular exudate, partly by loose plugs of fibrous tissue which lie in the air cells. There is a constant attempt at the production of a firmer wall by the proliferation of fibrous tissue cells, but when the bacteria are very virulent and abundant and the resistance of the individual slight, as in the case of *phthisis florida*, continued extension of the cavity may occur. Such a cavity usually contains a considerable quantity of residual fluid and caseous material in which a great variety of bacteria and occasionally even moulds and fungi may be demonstrated. This abundant flora has been extensively studied by Stephen Artault and others,[1] and there has arisen some question as to the part played by the tubercle bacillus in the production of the lesions. The weight of evidence is in favor of the idea that the whole process, as far as complete caseation, may be and is produced by the tubercle bacilli alone. The liquefaction of the caseous material may, however, result from a secondary infection, and it is apparently quite true that many of the symptoms—fever, general evidences of intoxication, etc.—which arise in the late stages after the cavity has become further infected, through its wide communication with the bronchus, are largely dependent upon the presence and growth there of other organisms.

The walls of the cavity are, as a rule, not smooth, but roughened by the irregularities of the necrotic substance. Further, there are usually prominent ridges or sometimes cord-like structures, stretching across, which on section are found to be bloodvessels whose walls are greatly thickened and very firm. They are on this account so resistant as to remain after the tissue around about them has been destroyed and removed, and they are quite isolated. Frequently they are entirely obliterated and on section are seen

[1] *Arch. de Parasitologie*, 1898, tome i.

to be merely solid cords of fibrous tissue. Sometimes they are eroded through and the ends hang free in the cavity. This type of obliterating endarteritis is obviously a protective process, preventing hemorrhage from even the larger vessels, which would otherwise be rapidly opened by the ulcerative process. Occasionally, the advance of the destructive process is more rapid than the obliterative change in the vessels and a severe hemorrhage may be the result. The bronchi usually stop abruptly as they enter the cavity, their walls having been destroyed. They may be somewhat dilated, but, as a rule, especially in the rapidly destructive cases, the changes which are evident in those portions of the bronchi which remain consist chiefly in the ulceration of their walls; the shallow ulcers pass into the mucosa and submucosa and leave a rough, raw surface within the bronchi.

The cavity, which is most commonly in the upper lobe of the lung, although by no means always so, may involve practically the whole lobe, or by extension nearly the whole lung. Such large cavities are always associated with abundant tubercles and areas of tuberculous pneumonia in the remainder of the lung. Often the lung is reduced to a mere sac, of which the thickened pleura forms practically the only wall, all the lung substance having been destroyed. Occasionally, if the pleural cavity has not been obliterated by adhesions, a perforation may take place through this thin wall, with the escape of fluid and *air* into the pleura. In every instance of such extensive cavity formation there is tuberculous pleurisy, but in such a case the admixture of air and abundant foreign bacteria and necrotic material sets up a *pyopneumothorax.*

Death is not necessarily the immediate result when such destructive processes occur in the lung. Indeed, the tendency toward healing, which is recognized in the attempt at encapsulation of the lesions, is often given play by the continued life of the individual, so that extensive scar formation takes place and the consistency and appearance of the lung may be greatly altered.

It has been mentioned that in the tuberculous pneumonia, etc., the substance of the lung tissue, the walls of vessels and bronchi, and the septa between the air cells become much infiltrated with cellular exudate. Perhaps in consequence of this intimate affection of the tissue the fibrous tissue is stirred up to proliferation and the walls of the air cells become thickened. Such general thickening of the tissues, which in course of time become very firm and scar-like, is often spoken of as indurative or interstitial pneumonia, and although it is found in connection with other infections is perhaps most commonly seen in tuberculosis.

In certain instances the walls of the air cells become so thick and rigid that they are no longer capable of distention, and the lining epithelium wherever it is preserved returns to its embryonic high cubical form so that the air cells come to look almost like the acini of a gland. Sometimes, indeed, they are widely separated by thick bands of fibrous tissue. Such an indurated lung is firm and elastic and has a grayish-black color. In the cases where the power of resistance of the individual is sufficient to allow of such a scar formation, the caseous areas and cavities usually become well walled off, although it is self-evident that in such individuals the cavities and caseous areas could hardly reach the maximum extent. Actual healing may be accomplished or the tuberculous areas at least so far encapsulated as to be rendered practically harmless. The same thing may, under exceptional conditions, occur in the case of cavities of considerable size, which then

become cleaned out, and all the necrotic material expectorated, leaving a smooth, firm, fibrous wall, over which epithelium grows from the bronchus. This, however, must be regarded as unusual.

All possible combinations of destruction and induration or protective changes may be observed in the lungs of phthisical individuals, the predominance of one or other condition at autopsy indicating with fair certainty the degree of rapidity with which the disease progressed as well as the power of resistance of the individual and the virulence of the bacteria. It may be repeated, however, that the commonest picture in any great series of cases is that in which at the apex or in the subapical region there is a cavity in open communication with a bronchus and demarcated from the adjacent lung by a layer of tuberculous granulation tissue, while in the lower portions of the lung there are areas of varying size usually ranged in clusters around the bronchi, in which the lung substance is consolidated, and in part, at least, caseous. These may be purely pneumonic in character, in the freshest cases, or in others they may be indistinguishable from conglomerate tubercles, but in most instances they are recognizable as caseous pneumonic areas in the margins of which tubercles and tuberculous granulation tissue have developed. It is, however, to be emphasized that tuberculosis of the lungs is in most cases a chronic affection of some duration, and that, therefore, the indurative changes are generally present.

Although tubercles of various forms and sizes occur regularly in connection with the tuberculous processes which affect the lung, sometimes as the basis of a tuberculous granulation tissue about the pneumonic areas produced by the bacilli, sometimes independently, from the local distribution of the bacilli, the diffuse miliary tuberculosis of the lung is generally the result of the entrance of the bacilli into the blood stream. This is shown by the fact that such lesions are all of the same size and age, and are distributed as is only possible by the agency of the blood stream. Further, owing to the width of the capillaries of the lung, it is unusual to find a typical diffuse miliary tuberculosis of that organ which is not part of a generalized miliary tuberculosis. In its origin, therefore, miliary tuberculosis of the lung agrees with most forms of generalized miliary tuberculosis, although the intensity of the process in the lungs may differ from that in other organs. Thus, when the tuberculous lesion which invades the bloodvessel pours its bacilli into a systemic vein or into the thoracic duct the lungs are the first to receive and sift out the bacilli. On the other hand, when the invading lesion affects a branch of the pulmonary vein the systemic organs first receive the bacilli. It must be remembered, however, that the bacilli are so minute that they pass fairly readily through any capillaries, and there need, therefore, be no very striking differences in the character of the lesions in the lungs and systemic organs, no matter what the point of entry of the organism. Thus, in a recent case in which a mortar-like, soft, caseous mass projected into a branch of the pulmonary vein the lungs and systemic organs were alike the seat of a fresh outbreak of miliary tubercles.

The freshest miliary tubercles in the lung may present the characteristic structure. Quite frequently, however, they show a pneumonic reaction even in the early stages, the alveoli about the point of localization of the bacilli in the capillaries of the alveolar wall being filled with desquamated epithelial cells and cells of leukocyte type exuded from the vessels. Indeed, it seems doubtful whether an absolute distinction could be drawn between

the miliary tubercles of the lung, arising from the introduction of tubercle bacilli through the blood capillaries and those which could result from the accession of scattered tubercle bacilli to the air cells.

The miliary tubercles often remain discrete so that the lung is readily insufflated and the intervening air cells are still functional, but they may become confluent and caseous. Ordinarily, however, the patient does not survive long enough for any extensive changes to occur, although cases are occasionally seen in which the tubercles scattered everywhere through the lung have actually become healed and converted into a firm, hyaline, fibrous tissue.

Still other possibilities exist in the development of tuberculous lesions in the lung, for it is not infrequent to find, in the absence of the extensive areas of pneumonia or cavities, single, isolated, caseous nodules, which are spherical in form and tightly enclosed in a dense, deeply pigmented capsule; sometimes these are calcified and may have the consistence of friable pebbles embedded in the lung. They seem to indicate a considerable degree of resistance on the part of the individual, in whom further extension of the process has been so promptly arrested. Sometimes these nodules reach a large size, and they are doubtless often regarded as gummata of the lung. In most instances, however, the history and the infectious nature of the lesion on inoculation into a guinea-pig will reveal the true character of the change.

**Tuberculosis of the Pleura.**—In all cases of active tuberculosis of the lungs when the lesion approaches the surface there is involvement of the pleura. In certain cases, however, there is no very conspicuous lesion in the lung; sometimes an adjacent caseous lymph gland or other tuberculous lesion by extension gives rise to the process. Whether a tuberculous pleurisy may arise in the complete absence of tuberculous lesions in the adjacent tissues seems very questionable.

Anatomically, the tubercle bacillus may produce directly or indirectly a great variety of lesions in the pleura and all transitions may be observed between the dry, fibrinous form, in which without the presence of any fluid exudate the pleura has lost its gloss, and the most advanced tuberculous empyema. Recent writers tend more and more to look upon pleurisy which begins without apparent cause and without definite pulmonary lesions as tuberculous in origin. These are the so-called idiopathic pleurisies, but careful search will usually reveal some associated lesion generally of tuberculous character, or with the lapse of time widespread and definite tuberculosis may appear. Peron has shown by bacteriological studies the predominant tuberculous nature of such pleurisies, and Aschoff, by inoculation of the exudate into guinea-pigs, was able to produce tuberculosis in the animal as often as by the inoculation of material from definite tuberculous pleurisy.

Peron distinguished two types of tuberculous pleurisy, the pleuritis tuberculosa serofibrinosa and empyema tuberculosa, although there are of course all intervening forms. The anatomical changes are fundamentally identical with those seen elsewhere. Over an area of tuberculous inflammation of the lung there may appear a local or quickly generalized fibrinous exudate, thick enough at times only to destroy the gloss of pleural surface, or in other cases to be pulled off as a thin, coherent layer. If the lesion in the lung be small and, as in the case of the apical foci, soon undergoes a healing process, the pleural exudate may also disappear or leave behind it an area of fibrous thick-

ening or adhesion with the parietal layer. In other cases the whole pleura may be rapidly involved. Fluid sometimes to a bulk of two liters or more may appear, with great compression of the lung. An exudate of fibrin and leukocytes, frequently very hemorrhagic in character, may be associated with this, soon to be encroached upon and in part replaced by the tuberculous granulation tissue, which springs up and leads to the great thickening of the pleural layers. In other cases the fluid is less abundant, and instead of being merely turbid is thick and creamy, with ragged shreds of fibrin and later caseous or necrotic material.

The tuberculous granulation tissue which lines the cavity becomes gradually thicker and denser, and except superficially loses its striking tuberculous character, so that it appears merely as a very hard, fibrous tissue. This usually goes hand in hand with the process of fibroid induration in the lung described above, and when, as is usual, the two layers of the pleura thus thickened become bound together, the result is that the indurated lung is extremely firmly united to the chest wall.

Occasionally when the pulmonary lesions are rapidly destructive, the pleura may quickly come to form the only wall of a large cavity in the lung, all the lung tissues having been destroyed. If the pleural layers are tightly bound together, this may be a safe-enough condition, but sometimes they have not so completely effaced the pleural cavity, and with the advance of the erosion of the tissue the cavity may be open into the pleura by a hole in this thin wall. Then the content of the cavity, usually by that time infected with various organisms, is poured into the pleura and a violent acute pleuritis is thereby occasioned. Since the cavity is in communication with a bronchus, air enters into the pleura and the condition of *pyopneumothorax* arises. The air may pass in and out freely, but usually there is a sort of valve action, so that while it passes easily into the pleura, it does not so easily escape. As a rule, since this condition arises only after extensive destruction of the lung, it may be regarded as practically a terminal process.

**Tuberculosis of the Lymphatic Tissues.—The Tonsil.**—Much has been written of late upon the relation of the tonsil to tuberculosis, especially with regard to its importance as a portal of entry, but even yet after the study of hundreds of cases there is no great unanimity of opinion. That the tonsils become infected by the tubercle bacillus is undoubtedly true, commonly in connection with pulmonary tuberculosis, but sometimes primarily. As to the frequency of its involvement we may quote the figures of Piffl and Rethi. Rethi found primary tuberculosis 6 times in 100 cases, while Piffl found 3 certain cases in his series of 100 cases. Much depends upon the method of examination, for while by inoculation Dieulafoy found numbers of tuberculous tonsils, Cornil by microscopic study as well as inoculation (but excluding the infected surface of the tonsil) found only 4 cases of tuberculosis in 70.

Secondary to pulmonary tuberculosis it is not uncommon to find the tonsils set with conglomerated tubercles, and ulcerated or caseous. Occasionally, lupus or superficial tuberculosis may extend from the mouth, which as in the nose gives rise to tumor-like nodules, and may later shrink away and leave scars. More important than these, from the theoretical point of view, are the cases of latent or inconspicuous tuberculosis of the tonsil, in which merely an hypertrophy of the tonsil or even no change at all is present. Such infections may take place from the air, sputum, or food,

and may give rise to tuberculosis of the cervical and mediastinal glands, and thus to a generalized tuberculosis. Grober, in studying the dissemination of bacilli from the tonsil, concludes that it is quite possible that tuberculosis of the apical vault of the pleura may be due to direct transportation of the bacilli from the tonsils, and suggests that the apical lesions of the lung may arise in the same way, that is, by way of a primary tonsillar affection, with secondary tuberculosis of the cervical glands and tuberculous pleural adhesions.[1]

**Tuberculosis of the Lymph Glands.**—When definite anatomical tuberculosis of the glands is demonstrated there can be no dispute as to the nature of the condition, but a series of cases appears to exist in which definite proof of the tuberculous nature of the swelling of the glands is not brought forward, but in which there is still the general impression that the whole condition is of a tuberculous nature. Such cases are classed roughly under the name of *scrophula* or *scrofula*, a name formerly much more used than at present, which has fallen somewhat into disrepute. This condition, which occurs chiefly in children and young persons, is characterized (Czerny, Blos, Neumann, and others) by general pallor, hyperplasia of the lymphoid tissue, especially about the throat, susceptibility to infections, and certain other special phenomena, such as circular caries of the teeth, phlyctenular conjunctivitis, and especially the seborrhœic eczema of the cheeks and the infantile prurigo (a nodular eruption which itches intensely and tends to suppurate).

There seems to be no clearly outlined anatomical basis for this conception of the condition. The changes described are thought to be due to some chemical poisoning, possibly by the toxins of the tubercle bacilli absorbed in some way (Solltmann suggests its absorption from the placental blood in intra-uterine life) which makes the child prone to infection and the development of definite tuberculosis. Possibly the determination of the opsonic index in such children might shed a clearer light upon the nature of the change. The term is apparently used in recent years to express a general condition and not to describe the actual lesions in the lymph glands, resulting in their caseation and adhesion with the surrounding tissue, for these are undoubtedly definitely tuberculous.

The clearly tuberculous lesions may well attract more attention. In general the glands become infected by the absorption of tubercle bacilli from a tuberculous lesion in tissues drained by their afferent lymph trunk, or by the transportation of tubercle bacilli as inert dust-like bodies along this afferent track until they are entangled in the lymph sinuses or in the lymph nodules of the node. Thus the bronchial glands at the hilum of the lung may become tuberculous from the absorption of bacilli from tuberculous lesions in the lung, or they may be infected by bacilli which have been drawn into the lung with the inspired air and which instead of producing any lesion in the lung have been taken into the lymphatic channels which course through the lung and transported to the bronchial glands, where they first show their injurious activities. The lesions produced in the gland are, however, not always the same, and it was this difference in their appearance which led to the difficulties of pathologists in interpreting them.

In some cases the glands become greatly swollen and firm, and on section

[1] *Klin. Jahrb.*, 1905, Band xiv.

show a surface mottled with yellow patches or uniformly yellow, opaque, and dry throughout. The cut surface is perfectly smooth and the substance is friable and crumbly. Such were the glands often spoken of as scrofulous. They frequently soften into a fluid consistence and the surrounding tissues may be affected by this process, a widespread inflammation of the capsule and adjacent tissue being set up. Villemin, Cohnheim, and others showed that they are infectious and on their inoculation tuberculous lesions result in the animal thus treated. Koch could find tubercle bacilli in them and microscopic examination often revealed tubercles around the margin of the caseous area, but still the idea of scrofula as something different from tuberculosis persists.

On the other hand, another condition occurs in which the glands become swollen and fairly firm. On section they are grayish and rather succulent, and are studded with gray, translucent nodules which, however, may later become conglomerate and undergo caseation and softening, as in the previous case. This has always been recognized as tuberculosis of the glands.

The two appearances are fundamentally identical. In the first instance the introduction of the bacilli in numbers causes a diffuse injury and a diffuse exudation of phagocytic cells with proliferation of the epithelioid connective-tissue cells. With the appearance of caseation the tissue at the margin of the caseated area always shows the abortive tubercles, which are also to be found about the areas of caseation in the acute pneumonic phthisis. In the second case the scattered groups of bacilli react upon the adjacent tissue in the ordinary way to produce tubercles. Tuberculosis of the lymph glands with caseation is particularly common in the neck, and especially in negroes in this latitude. The channels of infection have already been discussed and the portal of entry may exist anywhere in the upper respiratory tract or in the mouth, the masses of lymphoid tissue situated there probably acting as the direct transmitters of the bacilli. The glands become much enlarged and firm, so that great packets of them may stand out on each side of the neck below the angle of the jaw. With the extension of the caseation the capsules become inflamed, and the glands finally quite tightly bound together and to the neighboring tissue, so that their operative removal may offer great difficulties. In many cases the caseation and liquefaction may end in rupture into the intermuscular tissues, and the discharged material then burrows its way until often the skin is uplifted and finally broken through. A fistulous opening reaching down to the old packet of glands is the result of this discharge, and this becomes lined with thick, tuberculous granulation tissue, which shows little tendency to healing, which is often long delayed and sometimes only temporary. When it does occur it leaves a great, unsightly scar.

In connection with tuberculosis of the glands of the neck, involvement of the axillary and mediastinal glands is not uncommon and large packets of tuberculous glands may occasionally be found in the axilla without definite involvement of the cervical series. These are possibly, in some cases at least, due to tuberculous infections of the hand or arm. In the inguinal region groups of enlarged and caseous glands may occur secondary as a rule to tuberculous lesions of the genitalia, although in several instances tuberculous cutaneous alterations in the foot and ankle seem to be the origin.

The glands most commonly tuberculous are doubtless those situated at the hilum of the lung about the bronchi. These receive the materials

absorbed by the lymphatics of the lung, and with them often tubercle bacilli. They, like the glands of the mesentery, may thus receive tubercle bacilli when the general health of the patient is good, and perhaps this may account for the fact that they especially frequently contain completely encapsulated or fibroid tubercles, or sometimes calcified nodules, which represent obsolete tuberculous lesions. With the advance of the caseous process in these glands, bronchi or bloodvessels may be eroded and the bacilli emptied into them, with results recorded above. Similarly tuberculous pericarditis is often the result of the rupture of adjacent tuberculous glands. Tuberculosis of the mesenteric and retroperitoneal and other abdominal lymph glands is largely a consequence of tuberculosis of the digestive tract or at least of the absorption of bacilli from the intestinal tract, for it must be repeatedly emphasized that the bacilli are not always ready to destroy the tissue, but may behave, in their passage through such tissue as the intestinal wall, as inert particles and leave no trace of their passage. In children it is not uncommon to find the glands in the mesentery swollen into tumor-like masses which on section are found to contain a soft, cheesy material. This is the so-called *tabes mesenterica*, in which there is usually an associated widespread tuberculosis if the child lives long enough, but in which the abdominal tuberculosis is undoubtedly the oldest lesion. Occasionally in adults this form of tuberculosis may occur, with really enormous, firm mesenteric glands, and sometimes with packets of indurated glands along the aorta. In horses and sometimes cattle the same condition occurs. These glands, like the bronchial group, are prone to become calcified if the caseous material is not quickly softened, and we have observed instances in which, with a complete disappearance of active tuberculosis, the mesentery was distorted by the presence of large, irregular, stone-like masses, which replaced the glands.

Tuberculosis of the *lymphatic channels* themselves is rarely observed except in the thoracic duct and the intestinal and mesenteric lymphatic vessels, probably because sufficient attention is not directed to them. In the walls of the intestine the lymphatic channels which drain the area involved in tuberculous ulceration of the mucosa are usually distended and rendered conspicuous by the development of tubercles in their lining in such a way as to obstruct the flow of chyle. The tubercles are usually visible, both there and in the adjacent peritoneum, but the lymphatics are especially prominent on account of the stasis of the white chyle produced by their presence obstructing the lumen. In the thoracic duct the effect may be similar, as tuberculous nodules develop in its intima and partially occlude its lumen. They soon become caseous, and the disintegration of these masses gives rise to an infection of the venous blood and the inevitable development of a miliary tuberculosis.

In many cases in which no definite tuberculous lesion of the wall of the thoracic duct is discernible, but in which caseous processes in the mesenteric gland or tuberculous ulcerations in the intestine occur, tubercle bacilli may be found in numbers in the contents of the thoracic duct, and are apparently being swept into the blood without affecting the channel itself.

**Tuberculosis of the Circulatory System.—Pericardium.**—Tuberculosis of the pericardium, while less common than that of the pleura and peritoneum, is by no means an unusual affection. It exhibits a great variety of forms, all of which, however, are in principle much alike. In cases of generalized miliary tuberculosis the pericardium may become studded with miliary tubercles.

What is more generally regarded as tuberculous pericarditis, however, is not merely part of a generalized process. The tubercle bacilli gain access to the pericardial cavity most frequently from the adjacent pleura and lung in cases of pleural and pulmonary tuberculosis, but in many other instances they are introduced from adherent caseous lymph glands. In some cases it is difficult to trace the course of the infection and there may even be no distinct focus of tuberculosis elsewhere. In the earliest stages the tuberculous pericarditis may closely simulate a serofibrinous percarditis of non-tuberculous character, so that it is difficult to be sure of its tuberculous nature with the naked eye alone. In a recent case of this kind the surface of the pericardium was everywhere covered with a corrugated fibrinous layer, while the pericardial cavity was widely distended by a great quantity of perfectly clear fluid. Only the closest examination of the vertical section of the epicardium, which revealed here.and there minute tubercles, made its nature clear. In other instances hemorrhages may occur and the fluid exudate is blood-stained. In others it is rendered thick and turbid by flakes of fibrin and cellular exudate. Tuberculous granulation tissue is soon associated with the fibrinous exudate and is thickly studded with tubercles. With the advance of time the caseation of this tissue ensues and the caseous material is added to the rest of the exudate. Ordinarily a sufficient accumulation of fluid to keep the pericardial layers well apart is found only in the more rapidly developing cases, and therefore in the more chronic forms the apposed surfaces become adherent at least in places and later firmly bound together by the thick growth of tuberculous granulation tissue, throughout which caseous foci may be observed. In several specimens recently observed at autopsy the parietal pericardium was closely bound to the heart, and on section a mass of partly caseous tuberculous granulation tissue, fully 1 cm. in thickness, intervened between the visceral and parietal layers. In another case the caseous substance had become liquefied, so that it escaped on incising the thick covering of the heart, leaving irregular, burrowing canals, which ran in the substance of the pericardial adhesions around about the heart. In other cases the adhesions may become very firm and scar-like, with caseous patches rather sparsely scattered and sometimes calcified. Whether a tuberculous infection of the pericardium may heal and give rise to a clean, fibrous, adhesive pericarditis is difficult to determine. Meltzer has described a form of tuberculous pericarditis in which firm nodules were found similar to those in the perlsucht of cattle.

**Myocardium.**—Tuberculosis of the myocardium is far less common than the analogous disease of the pericardium. It is, however, probably more common than is usually supposed, especially in the form of a diffuse miliary tuberculosis, which forms part of a generalized miliary tuberculosis. The frequency of this condition was first pointed out by Weigert, and Pollak has since reviewed the subject.[1] It has probably no clinical significance. Another form consists in the appearance of large, solitary caseous masses in the myocardium, which may sometimes project into the cavity of the heart. A diffuse interstitial myocarditis with giant cells, but without caseous foci, is also described, but the bacilli must be demonstrated in such a case to prove its tuberculous nature.

**Endocardium.**—Tuberculosis of the endocardium occurs either as scattered tubercles in the endocardial lining of the heart or as actual tuberculous vegeta-

[1] *Ztschr. f. klin. Medicin*, 1892, Band xxi.

tions affecting the valves or extending on to the walls of the chambers. The tubercles when miliary in form are usually subendocardial, according to Benda. They appear as minute white spots usually in the conus arteriosus of the right ventricle, and on section show the ordinary typical structure of a miliary tubercle. In a recent case no giant cells were found even in a series of sections, and the endothelium was fairly intact over the tubercle. Actual tuberculous vegetations upon the valves have been found to contain tubercles and tubercle bacilli, and are explained as due to the implantation of the bacilli upon the valves, but these cases are rare. Any of these processes may aid in the further dissemination of the tuberculosis.

**Vessels.**—Mention was made of the tuberculous affections of the vessels in speaking of the origin of general miliary tuberculosis. Benda has pointed out that at least two distinct types of tuberculous lesion of the vessels may occur: one in which the adjacent caseous tuberculous focus encroaches upon the vessel from without and finally may erode even to the point of discharging caseous material into the lumen of the vessel, and the other in which the bacilli are deposited from the blood stream upon the intima and there produce a tubercle which becomes covered with a thrombus and may later undergo caseation and softening. Such intimal tubercles are found in the aorta (Blumer, Longcope, etc.) and smaller arteries, as well as in the veins and thoracic duct. An example was recently seen in a pulmonary vein into which the rounded caseous mass projected from a branch which it completely occluded. This caseous mass was in part overgrown by endothelium and fibroblasts, but it was entirely within the internal elastic lamella, there being only a slight new-growth of epithelioid cells and occasional giant cells outside that membrane.

To these two forms Chiari adds a third, produced by the transportation of bacilli into the vasa vasorum. It is possible that the adventitial tuberculous lesions of the bloodvessels in tuberculous meningitis may arise in this way, but there is also the possibility that the lymphatic channels in the vessel walls form the channel of infection, while Hektoen and others regard these vascular changes as due to bacilli which are brought by the blood stream of the vessels themselves. The lesion in such a case usually affects the adventitia more intensely than the intima, and leads to the formation of an eccentric caseating nodule in the vessel wall. Perivascular tuberculous lesions developed in the lymphatics of the vessel wall are by no means uncommon in the lung in cases of extensive pulmonary tuberculosis, as recently emphasized by Letulle.

Probably the most frequent tuberculous affections of the vessels belong to the first group. Extension of the caseating process takes place just as elsewhere, there being always a proliferation of epithelioid cells in advance. In the case of small vessels, and indeed of all vessels when the process advances slowly enough, an obliterative endarteritis arises, which protects the vessel by obliterating its lumen or by thickening the wall in front of the necrotic area. In other cases the wall of the vessel is weakened by the erosion, and the pressure of the blood bulges it out at that point into a sort of small, aneurismal sac. Such are the altered vessels which on bursting at this dilatation give rise to extensive pulmonary hemorrhage. If the vessel be approached by a caseous area of small extent and completely encapsulated, as, for example, a lymph gland with central caseation, a communication may be established through the vessel wall with this caseous

area and an eddying current of blood will wash the caseous material out into the blood stream. Further, if the vessel attacked be a vein of considerable size and not obliterated, the tuberculous caseous material may extend into its lumen, and by crumbling away set free great quantities of tubercle bacilli into the passing blood, which will ordinarily go to produce an acute miliary tuberculosis.

Interesting and important is the relation of tubercle formation in general to the small bloodvessels. It has been pointed out that a stimulus which sets up the production of a tubercle nodule does not excite the new formation of bloodvessels, and that those which are by any chance included in a tubercle soon become obliterated and disappear. Nevertheless, the ordinary tuberculous granulation tissue shows the presence of abundant capillary loops; indeed, it differs in no respect except the presence of the tubercles and the tendency to caseation from other granulation tissue.

**Tuberculosis of the Digestive Tract.—Mouth.**—The mouth is not commonly the seat of tuberculous affections, still there have been reported cases in which the lips, gums, edges of the tongue and palate, as well as the fauces, were infiltrated and ulcerated. Tuberculous ulcerations in these situations have the same character as elsewhere; they are irregular in outline, with somewhat indurated or undermined edges, and with uneven base, frequently showing small, caseous nodules. Such ulceration is very rarely primary, but is usually secondary to pulmonary tuberculosis. In connection with caries of the teeth, however, direct infection may occur and even extend to the adjacent alveolar process of the jaw. As in the case of the nose, pharynx, and tonsil, lupous granulations which have extended from lupous areas on the skin may occur in the mouth.

**Œsophagus.**—Tuberculosis of the œsophagus is also extremely rare; possibly largely because of the very smooth lining, which gives no foothold to organisms, and partly because of the rapid transit of infectious materials. Infection may, however, occur from food containing bacilli or by swallowing tuberculous sputum, and the result is the production of nodules which ulcerate sometimes quite deeply. The œsophagus may be involved in a generalized miliary tuberculosis, but the other important type of tuberculous lesion is that in which it is affected from without and encroached upon by an advancing tuberculous process, either in adjacent lymph glands or pericardium or pleura. Even caseous areas in the lung may become adherent and cause erosion of the wall of the œsophagus.

**Stomach.**—The rarity of tuberculous ulcers of the stomach is attested by Simmond's figures, in which among 2000 autopsies upon tuberculous patients 8 cases were found. Glaubitt's percentage is higher, as among 2237 such autopsies he found 47 cases of tuberculous ulcers. Various explanations for the relative immunity of the gastric mucosa have been given. The antiseptic action of the gastric juice is apparently regarded as the most important factor, for, although as shown by the common ulcers in the intestine which result from the deglutition of sputum in tuberculosis of the lungs, the bacilli are not killed by the gastric juice, they are still prevented from settling and growing in the mucosa. An injury to the mucosa affords chance for such localization, and any lesion which by pyloric obstruction or in any other way causes a diminution in the acidity of the gastric juice will set up conditions which greatly favor tuberculous infection.

Several distinct forms of tuberculous affection of the stomach occur.

As part of a generalized miliary tuberculosis nodules appear in the gastric wall, doubtless with considerable frequency. Willms has described in detail tuberculosis of the stomach in which the walls were thickly studded with small tubercles. Solitary tubercles or encapsulated tuberculous foci may occur rarely in the stomach wall, and one such case has been reported recently by Van Wart. The stomach may also be approached from without and eroded by a caseous tuberculous mass. Finally, there are the ulcerations, sometimes single, often multiple, which doubtless arise from the direct deposition of bacilli from swallowed infectious material. The ulcerations are usually rather small, with irregular outline, elevated, somewhat undermined, indurated margin and rough base, sometimes with tubercles. Such an ulcer may in rare instances extend deeply and erode a vessel. Tubercle bacilli may be demonstrated in these ulcers, although the diagnosis is more certainly established by a histological examination, for it is not impossible that tubercle bacilli from the swallowed sputum may adhere to the surface of an ulcer.

**Intestines.**—Tuberculosis of the intestine is both absolutely and relatively of frequent occurrence, the lesions being rarest in the duodenum, and occurring more abundantly as one passes toward the ileocæcal valve, where they are only less common than tuberculous lesions of the lungs. In the colon some evidences of tuberculosis are usually found whenever the small intestine is diseased, and sometimes there are ulcerations there when there are none in the ileum.

As to the mode of infection it may be stated that, with the exception of certain cases, especially in children in whom the tubercle bacilli reach the intestine with such food as milk, they are nearly all secondary to tuberculous infection elsewhere in the body and especially in the lungs. When there is a cavity in the lung it is obvious that the swallowing of bacillus-holding sputum will tend to the infection of the intestine.

It is an interesting question as to whether the bacilli may really be transported like inert particles of dust through the intestinal wall without leaving a noticeable trace behind them. Such is apparently the case in the lung, in which the bronchial glands may show the first lesion, although the bacilli are apparently received by the way of the lung. Von Behring, indeed, makes great use of this possibility in his explanation of tuberculous infection in general in sucklings. In suckling infants he shows that certain proteids may pass the intestinal wall unchanged, and, indeed, that such bacteria as anthrax may reach the circulation and give rise to a general septicæmia, although they pass along the intestinal tract of adult animals without being thus absorbed. Reasoning in the same way he believes that in newborn infants tubercle bacilli may be received in the milk, and pass directly through the intestinal wall to some distant tissue, perhaps the mesenteric lymph glands, where, after lying latent for a long time, they finally give rise to a spreading tuberculosis. Von Behring apparently ascribes many cases of tuberculosis developing in young people to the beginning activity of tubercle bacilli, which taken in the food at an early period passed the intestinal wall without causing a lesion and remained latent in the tissues.

Infrequent and ill-defined as these cases of primary tuberculosis of the intestine are, those which are due to the swallowing of tuberculous sputum are common and familiar. The bacilli adhere to the mucosa and work their way into its substance. Orth holds that the lesions begin always in the lymph nodules, but it is difficult to be sure that the bacilli do not occasion-

ally produce their first effects elsewhere in the mucosa. The first change is in the appearance of tubercle nodules in the substance of the mucosa and very frequently in the lymphoid nodules or Peyer's patches. These tubercles soon become confluent and undergo caseation and softening, and finally setting free their soft contents into the lumen of the intestine, an ulcer is left, the base of which is covered with necrotic tissue. Such ulcers may at first be small and round and appear as punched-out cavities in the centres of enlarged solitary nodules. Later, with the extension of the tuberculous process, they become larger and ragged in outline, bounded always by a rather prominent, elevated margin which is sometimes undermined. The base is still covered with grayish, opaque material, but frequently shows minute translucent or opaque, yellowish nodules. Such nodules are also to be seen and felt in the margin of the ulcer, and by their confluence and continued caseation they occasion the extension of the ulcers. The intestinal wall may be eroded to varying depths, and sometimes a tuberculous granulation tissue studded with tubercles is formed in the submucosa and constitutes the base of the ulcer, at least for a time. In other cases, while this granulation tissue is to be found at the margins and in the substance of the wall, the muscular bundles are laid bare in the floor of the ulcer. Indeed, with rapid advance of the process the musculature may be eroded and the intestinal wall finally perforated so that the contents escape into the peritoneum; more often with the advance of the tuberculous ulceration there is such a thickening of the intestinal wall and such formation of adhesions that if the wall is finally perforated the contents are kept from the general peritoneal cavity by the adhesions. Communication may be set up between adjacent loops of bowel in this way, or intraperitoneal fæcal abscesses or even a false anus may arise.

Tuberculous granulation tissue prone to caseation forms throughout the wall about the ulcer and in the subserous tissue nodules of the characteristic type soon appear, often in great numbers, so that the position of the ulcer is plain from the outside on account of the vascular granulation tissue and opaque or translucent nodules which accumulate opposite the ulceration.

The ulcers may come to occupy the position of Peyer's patches, but more commonly their long axis lies more transversely, and in many cases the ulceration extends especially transversely so as to finally encircle the intestine and produce the so-called "girdle ulcers." This distribution obviously depends upon the course of the lymphatics in the intestinal wall, which are quickly invaded by the bacilli, and which in that way aid in the propagation of the tuberculous lesion, step by step, around the intestine. In the larger trunks of the lymphatic channels in the intestinal walls, tubercle bacilli settle and produce tubercle nodules which may occlude the channels at that point. Stagnation of the chyle then makes that lymphatic very conspicuous, and it is not uncommon to see the lymphatic channels running away to the mesentery, from the region of the ulcer, studded with gray or opaque nodules, between which the canal is greatly distended with opaque, yellowish-white chyle. Often these may be traced to the mesenteric lymph glands, which are themselves in such a case usually caseous or at least thickly studded with tubercles.

It seems probable that such a condition could readily occasion the abundant distribution of tubercle bacilli into the thoracic duct, which, even if no lesion of the thoracic duct arose, could go far toward the production of a generalized miliary tuberculosis.

In the lower end of the ileum, where stagnation of the fæcal material is favored, the ulcers become very large and confluent, so that often nearly the whole mucosa is destroyed. Even the intervening mucosa in such cases is not unaffected, being usually the seat of a catarrhal inflammation, which in the colon gives rise to the diarrhœa so common in this condition. In the appendix, tuberculous ulcers of the same character may occur and even go on to perforation. In the colon the ulcerations are more commonly irregular and rounded, although in certain cases they assume the girdle form. The healing of such ulcers is usually interrupted, if it begins at all, by the death of the patient, but sometimes the advance of the process ceases and scarring of the cleansed ulcer begins. The floor of the cavity contracts so as to bring the overhanging epithelial margins close together or even to push them upward into the intestinal lumen. Some new-growth of epithelium from these edges may take place, but the development of scar tissue is usually so great as to form the most prominent feature and to cause actual stenosis of the intestine when the ulcer is an extensive one of the girdle form.

The extension of tuberculous ulceration through the wall of the intestine commonly gives rise to fæcal abscesses in the neighboring tissue, or, if the conditions are favorable, to the extension of the burrowing to another cavity or even to the outer surface of the body. Thus, tuberculous infection of the mucosa of the anal portion of the rectum may cause in time the formation of a perirectal abscess, which on rupturing at the anus produces a fistula. The great majority of anal fistulæ have been shown to be of a tuberculous nature, the infection arising from bacilli which have been swallowed or which come from secondary ulcers higher up; the localization of these is favored by the excoriations of the mucosa of the sphincter region, which are so common. The canal is usually lined with very abundant tuberculous granulation tissue. Tuberculosis of the *anus* may also appear in the form of lupous granulations which have extended from the adjacent skin surfaces or even as one of the rarer papular tuberculides of the skin.

**Salivary Glands.**—Tuberculosis of the salivary glands, formerly thought to be extremely rare, has been reported recently in a large number of cases. The parotid is most frequently affected, the submaxillary less often, and up to the present there is no report of a case of tuberculosis of the sublingual gland. Infection may occur (1) by way of the general blood stream, in which case the salivary glands become the seat of miliary tubercles, just as do the other organs, or may show a more extensive caseating infiltration; (2) infection may occur along the course of the duct from the mouth, especially when favored by the presence of carious teeth; and (3) there may be extension of a caseous process from adjacent tuberculous lesions in lymph glands, bones, etc. The change in the gland in most cases appears either in diffuse form, with caseous infiltration and softening or subsequent scarring, or as a focal lesion, forming a caseous, encapsulated nodule.

**Pancreas.**—The pancreas seems especially resistant to tuberculous infection, and references to tuberculous lesions other than miliary tubercles are hardly to be found. Lefas describes two cases, but thinks that in those, too, the tuberculous process is really an affection of embedded lymph glands. Parenchymatous degeneration and interstitial sclerosis of the pancreas are often observed in cases of widespread tuberculosis.

**Liver.**—In sharp contrast with the pancreas stands the liver, in which tuberculous lesions are extremely frequent, being estimated by Simmonds as

occurring in 82 per cent. of the cases of tuberculosis which he studied. The lesions are, however, seldom extensive, but consist of the most part in extremely minute tubercle nodules, scarcely visible to the naked eye, but which tend to become confluent, so as to form small or miliary, caseous nodules. These nodules have the characters typical of the ultimate tubercle, as described above, and appear usually in the periportal connective tissue, later invading the substance of the lobule. They result from a transportation of bacilli by the blood stream, which can take place either through the hepatic artery, in which case they form part of a generalized distribution, or they may be secondary to lesions of the intestine or spleen, which distribute their bacilli into branches of the portal vein and thus into the liver. Klebs suggested that the bacilli may be carried along the lymphatics into the liver, but this seems improbable. The tubercles are smaller in the liver than elsewhere, probably because of the unfavorable action of this tissue of the liver upon the growth of the bacilli, although the attempts to determine this effect experimentally have so far failed. In the course of their growth they compress and destroy a considerable portion of the liver tissue and surround themselves with scar tissue. If the process last a sufficient time a definite cirrhosis of the liver may arise, in which the changes are quite analogous to those of the ordinary cirrhosis, the tubercle bacilli constituting the injurious agency which destroys many liver cells, and while these are replaced by scar tissue, stirs up the remaining liver cells to a compensatory hypertrophy. Anatomically, the presence of the tubercles may be the only point of distinction between these two conditions.

Larger or solitary tubercles may rarely occur in the liver, often near the capsule, sometimes in relation with the periportal connective tissue; commoner than these are the so-called gall-duct tubercles, as to the origin of which there has been so much debate. Many of the miliary tubercles mentioned above may be bile-stained, but these gall-duct tubercles arise near the bile ducts and directly invade their walls, so that there is soon an open communication between the caseous centre of the mass and the bile ducts; they assume the appearance of abscesses with green, semifluid contents. It is probable that these tubercles arise from bacilli brought in by the stream and perhaps transmitted back again by the lymphatics in the wall of the bile ducts, and that they develop outside the bile duct, invading its wall from without. Nevertheless, attempts have been made to show that they arise from the ascending infection of the bile ducts by bacilli from the intestine, and that they extend from the epithelial lining of the duct outward.

**Gall-bladder.**—Tuberculosis of the *gall ducts* and of the *gall-bladder* have been described in association with gallstones, the whole lining of the gall-bladder having been caseous in one instance.

**Tuberculosis of the Peritoneum.**—Various types of tuberculous peritonitis occur, conditioned apparently by the virulence and number of the bacilli and by their mode of entry, for while the less virulent seem to produce miliary tubercles and a great outpouring of fluid, the more virulent set up a rapidly destructive caseating process, with exudation of fibrin and many cells. The portal of entry for the organisms may be the blood stream or the intestinal wall in cases of tuberculosis of the intestine, or the Fallopian tubes in cases of genital tuberculosis or any caseous focus which may extend to the peritoneum. In all of these instances it is therefore secondary to some other lesion, but it seems to have been fairly shown that in some instances it may be the

only tuberculous lesion found, and it must be supposed that the bacilli are brought to the peritoneum without causing any extensive lesion elsewhere.

Anatomically, we may find minute miliary tubercles upon the peritoneal surfaces and hidden in the folds of the omentum without any remarkable accumulation of fluid or exudation of fibrin. The peritoneum over them looks quite smooth. In other cases there is a thin exudate of fibrin about them and a quantity of clear or slightly turbid fluid is present in the cavity, sometimes a great quantity sufficient to float up the intestines, which are then quite separate and free. In still other cases a rather vascular, grayish, translucent, tuberculous granulation tissue, thickly studded with tubercles and giving rise to friable adhesions between the intestinal coils, appears on the peritoneal surfaces. These adhesions are most marked when there is no accumulation of fluid in the peritoneum, and indeed they may become quite universal and bind the whole contents of the peritoneum into a dense mass which can hardly be disentangled without tearing the intestines. The omentum in such a case becomes tightly rolled and folded upon itself, so as to assume the form of a firm, solid mass of tissue, which stretches across the abdomen with the transverse colon. It is mottled with yellow and gray patches, which correspond with the alternating tubercles and remnants of fat. In course of time the tuberculous adhesions become the seat of extensive caseation and it is not uncommon to find secondarily formed spaces and canals burrowing between the coils of intestine in these adhesions. Frequently, such a matted condition of the peritoneal organs is the result of discharge of tubercle bacilli from intestinal ulcers, and the perforation of such ulcers into the adhesions may give rise to fæcal abscesses between the loops of intestines or to abnormal communications between adjacent loops.

Localized tuberculosis of the peritoneum is not uncommon, the bacilli apparently affecting the parts of the peritoneum, into which they can sink and rest quietly, such, for example, as the pouches of the pelvis and hernial sacs, which are very often tuberculous. On the other hand, the course of particles in the intact peritoneal cavity is predominantly toward the diaphragm, and hence it is common to find tubercles developing in great numbers on the under surface of the diaphragm.

Healing may occur, especially after operative interference, when the tubercles become gradually smaller and converted into a dense fibrous mass, apparently with the death of the bacilli. Whether the dryer types of peritoneal tuberculosis with extensive adhesions and caseation can heal is doubtful. It is in the cases with well-marked ascites that the best results have been obtained from operation. Every possible suggestion has been made in explanation of this fact, such as stimulus of the operation, exposure to air, production of venous stasis, relaxation of the tissue and improved circulation, exudation of antibacterial serum after the operation, etc. What seems the most plausible explanation is put forward by A. E. Wright, who finds that the fluid in these cases is poor in opsonic power as compared with the blood plasma of that patient, *i. e.*, it has little power to aid the phagocytes to engulf the tubercle bacilli. On its removal, however, new fluid, the blood plasma itself, enters the peritoneum, and by its high opsonic power greatly favors phagocytosis.

Healed types of peritonitis are sometimes observed, as in the instances in which the peritoneum over the liver, spleen, etc., is greatly thickened, even to the extent of contracting and compressing the underlying organ. This in

association with similar changes in the pericardium and pleura is usually regarded as tuberculous, but perhaps not upon very conclusive evidence. Healed caseous nodules hanging by long hollow stalks from the peritoneum were described by the writer.[1]

**Genito-urinary Tuberculosis.—Kidneys.**—Tuberculosis of the kidney may assume widely different forms according to the mode of introduction of the bacilli and other less well-defined factors. Only a few channels seem open to the bacilli in their entrance into the kidney, and of these the most obvious seem to be the blood stream and the ureteral tract and pelvis. It is true that Borrel claims invasion by way of the lymphatic channels, but this seems hardly plausible. It is, however, quite possible for a neighboring tuberculous lesion to extend to the kidney and produce a more or less localized tuberculosis of that organ.

In association with tuberculosis of other organs in which there has been some dissemination of the tubercle bacilli by the blood stream, it is not at all uncommon to find small tubercles scattered throughout the cortex or in the pyramidal portion. These may be very small and translucent, but more frequently they are conglomerated into masses which stretch in lines between the tubules and vertically to the surface of the kidney, and are soon caseous and opaque in the central part. They may sometimes reach a considerable size and undergo a central softening. They may be formed by the lodgement of tubercle bacilli anywhere in the tissue, just as in other organs; but Benda has described especially the formation of tubercles about glomeruli in which he finds twisted rolls of bacilli so bulky as to block the glomerular capillaries. About these, after a short time, an emigration of leukocytes occurs and later with destruction of the glomerulus the formation of a surrounding area of epithelioid and giant cells. This type of renal tuberculosis is of relatively slight importance, since it is usually associated with much more serious and destructive tuberculous lesions in other organs. In the kidneys of patients dying of chronic phthisis, however, one may sometimes find scars and depressions which by some are regarded as the remains of tubercles. Interesting and important in this connection is the occurrence of a chronic nephritis, with extensive degeneration of the epithelial cells and increased permeability of the kidney, which is apparently due to the action of a circulating toxin (Landouzy and Bernard).

There is another type of tuberculosis of the kidney which is usually associated with tuberculous lesions of the remainder of the genito-urinary system, but not necessarily with any general or disseminated tuberculosis. This is a localized process not necessarily affecting both kidneys, as in the other form, but beginning usually in the pyramids, where they lie adjacent to the pelvis and thence eating out the substance of the kidney until in some cases little of its tissue is left.

Its mode of origin is somewhat doubtful, although until recent years it had been quite generally held to be an ascending infection from tuberculous lesions of the remainder of the genito-urinary system, analogous to the pyelonephritis which follows urethral obstruction and cystitis. Recently, many writers, especially surgeons, maintain that it, too, is the result of the dissemination of the bacilli by the blood stream. Efforts to produce the condition experimentally have been almost entirely unsuccessful, although

[1] *Johns Hopkins Hospital Bulletin*, 1901.

Baumgarten by ligating the ureter with a thread infected with the bacilli has produced a similar affection. Injections of bacilli into the bladder or even into the ureter have usually failed, but the exact degree of obstruction necessary to success in those cases seems not to have been produced. Pels Leusden has recently attacked the problem from the other side and attempted the production of tuberculosis of the kidney by the injection of bacilli directly into the renal artery of one side. His results are as yet not convincing.

The age of the various lesions encountered in any case of genito-urinary tuberculosis are important in determining their relation to one another, and still the analysis of any considerable number of cases will reveal the great difficulty in drawing any definite conclusions upon this point. In many instances the process is so advanced in the kidneys, bladder, prostate, and epididymis that it is impossible to say which was first affected.

In the Johns Hopkins Hospital 36 cases have been studied at autopsy, in which one form or other of tuberculosis of the male genito-urinary system occurred; of these 19 showed tuberculous changes in the kidneys. Of these 19 cases there were only 2 which did not show coincident lesions of the genitalia, the prostate and epididymis being often the seat of lesions. In 2 cases there was tuberculosis of the kidney, in 1 case with tuberculosis of the ureter and bladder, in the other without either, and in both without changes in the genitalia. In none of the other cases could it be definitely stated that the lesions in the kidney were more advanced than those in the prostate or epididymis. In 13 of the 19 cases there was more or less extensive tuberculosis of the bladder, although the intensity of this lesion corresponded only in a general way with that of the process in the kidneys or in the genitalia.

Of the 36 cases, 29 showed tuberculous lesions in one or both epididymes, and 22 had caseous areas in the prostate. Of the 34 cases which showed tuberculosis in some part of the genital tract, in 19 the lesion seemed to be oldest in the epididymis, in 9 it was clearly most advanced in the prostate, while in 6 it had developed to about the same degree in both. The testicle was involved in 16 and the vesiculæ seminales in 17 cases. It seems entirely probable that the infection of the kidney, at least in men, may result from the transportation of the bacilli from an older lesion affecting the genital tract and bladder, in spite of the objection that it is difficult to explain this transportation against the stream of urine in the ureter. The mechanism is quite the same as in the cases of ascending pyelonephritis following infection of the bladder, and the entry of the organisms into the ureteral orifice is sometimes facilitated by the destruction of the soft tissue which guards (valve like) that orifice. Hæmatogenous tuberculosis of the kidney of this localized type is of course easily conceivable, but it would in most instances be necessary to admit that a hæmatogenous infection of the epididymis or prostate had also occurred some time before. In women the relation to genital tuberculosis is much less clear and there is less objection to the assumption of a hæmatogenous origin. However, it is the growing tendency among surgeons to regard these lesions in the kidney in men also as hæmatogenous in origin, and it may well be that the autopsy material alone does not furnish a fair view of all sides of the question.

The condition is less often seen at autopsy in women than in men (6 cases in women to 19 in men in this series), but the surgeons see many more cases which are diagnosed as tuberculosis of the kidney in women. It is most often unilateral, but in many cases it affects both kidneys and ureters.

The lesion seems to begin in the papillary portion of the pyramid, where in one of this series quite isolated, eroding tuberculous lesions were to be found, in the complete absence of tuberculosis of the rest of the urinary tract. Such cases speak strongly for the transportation of the bacilli to the kidney by the blood stream. Usually, when one examines the kidneys the tuberculous process has already involved the pelvis and some part of the ureter and has ulcerated away portions of the pyramids and adjacent tissues, hollowing them out into ragged cavities widely open into the pelvis and lined with a thick opaque layer of caseous material. Tubercle nodules may be visible in the walls of these cavities, and they may be also scattered about in the cortex of the kidney. Usually the pelvis is hyperæmic and covered with a partly caseous granulation tissue, or it may show extensive shallow ulcers and a much thickened and indurated wall. In these more advanced cases the pyramids may be completely destroyed and the cavities extend far into the cortex, so that only a thin layer of cortical tissue persists. In advance of this process there is always the new formation of tuberculous granulation tissue, and when the kidney substance is completely destroyed this may still form the wall of a cavity, which is sometimes much larger than the kidney itself. Indeed, in a recent case the large, tumor-like mass found in the position of the kidney proved to be composed of a group of sacs matted together and containing a caseous material, but only remotely resembling the kidney in form, all the kidney substance having been destroyed. Occasionally, the process may make even greater strides and give rise to a perirenal tuberculous abscess or to a fistula extending outward to the skin. When the patient's power of resistance is great there may be a more effective production of scar tissue and the process of caseation may be less rapidly destructive. One specimen of this type showed an enormous enlargement of the kidney, to which the thickened capsule was densely adherent; the whole organ was practically converted into a translucent fibrous tissue, in which were numerous pyramidal, ragged, caseous areas. The ureter was enormously thickened, the lumen being practically obliterated, but choked with caseous material. Another specimen showed rounded, caseous areas in the substance of the kidney, well encapsulated and sharply separated from the surrounding kidney substance. In still another there was great contraction of the kidney about a mortar-like, caseous mass which filled the pelvis and the eroded cavities in the kidney substance, the ureter being obliterated. The presence of other healed and healing tuberculous lesions makes it probable that this was a tuberculous process and not merely a softened renal calculus.

**Pelvis and Ureter.**—The lesions in the pelvis and ureter consist in the formation of tuberculous granulation tissue which undergoes caseation and ulceration, thus excavating the tissues of the wall. The walls of both pelvis and ureter usually become much thickened, so that the ureter may readily be palpated as a thick, firm cord. Of special significance is the damage produced by the ulceration of the mucosa about the ureteral orifice in the bladder, which destroys its valve action and renders regurgitation from the bladder possible.

**Bladder.**—The bladder may show a variety of lesions. Miliary tubercles may occur in the mucosa, usually about the trigonum or at the beginning of the prostatic urethra. In other cases slight erosion of the mucosa may be marked by the presence of abundant sticky, mucous exudate over the whole

surface. Widespread ulceration may occur either in the form of minute, closely set erosions covered with caseous material, which give the appearance of a diphtheritic exudate, or as shallow, irregular, ragged ulcers which destroy wide areas of the mucosa. These are sometimes deeper and erode the muscularis, even perforating the whole wall, when they usually give rise to fistulæ, extending to the skin or elsewhere. By marked contraction and thickening the bladder may be reduced to a very small size. Whether tuberculous cystitis can arise primarily is doubtful. It seems probable that it usually depends upon tuberculosis of the prostate and genitalia, although even if the lesion of the kidney be held to be the result of the tuberculosis of the bladder there is no reason why it in turn should not become more extensively infected from the kidney.

**Urethra.**—Tuberculosis of the urethra is very uncommon and the mucosa seems to have a certain degree of immunity from the invasion of the bacilli, for there are surely quantities of tubercle bacilli poured over it at intervals in every case of genito-urinary tuberculosis. In two such cases recently seen at autopsy there was extensive, almost continuous, ulceration of the urethral mucosa, the ulcers extending quite to the meatus. The flat ulcers were covered with a thick, caseous layer, and extended only into the underlying connective tissue. Tuberculous ulcerations of the glans penis and prepuce were not present in these cases, but have been frequently reported, usually as a consequence of infection during the ritual of circumcision from the saliva of the person officiating. The possibility of infection by coitus with a woman with genital tuberculosis has of course been suggested, but Franck in a critical review of the literature could find no credible instance of this.

**Prostate, Seminal Vesicles, Vasa Deferentia, Epididymes, and Testicles.**—The prostate, seminal vesicles, vasa deferentia, epididymes, and testicles are frequently tuberculous. The tubercle bacilli are brought to them either by the blood stream or by direct invasion from the urinary tract. The weight of evidence seems to favor the hæmatogenous origin of genital tuberculosis in the male from an older focus elsewhere, the point of predilection being commonly the epididymis, although both Krzywicki and Malinski make the statement that the prostate is in the great majority of cases first affected, the infection of the seminal vesicles, vasa deferentia, and epididymes being secondary.

Tuberculosis of the *testicle* is less frequent, and usually is distinctly the result of extension from the epididymis. When the lesions do occur there they appear as grayish nodules gradually undergoing caseation, or they may take the form of a gradually advancing area of caseation continuous with those in the epididymis. The tubercles form in the testicle in and among the tubules and show the characteristic structure. In the epididymis the lesion begins within the tubules and leads to the destruction of their epithelium, the tubules becoming greatly thickened and distended with a caseous debris in which fragments of nuclei are seen. Definite tubercles may develop in the neighborhood, and it is not long before in the greatly enlarged epididymis a coalescent, caseous mass represents all that is left of the structures. This may extend until adhesions with the skin of the scrotum are produced, and it is not uncommon to see sinuses leading from the skin into the cavity of the much altered epididymis and testicle, which by that time has usually been invaded. The tunica vaginalis may become infected and react as the peritoneal surface would under similar circumstances. The vas deferens

becomes filled and choked with caseous material, which is largely due to the infection and ulceration of its walls. In the seminal vesicles the infection may finally bring about very great distention of the cavities with an opaque, caseous material; disintegration of the wall may take place, but is not usual. Destruction of the tissue of the prostate is, however, not infrequent, caseous areas appearing through the substance of the gland, and by their liquefaction often leaving it riddled with cavities.

**Female Genitalia.**—Tuberculosis of the female genitalia has been described as a primary affection, but it is usually found as a sequence of tuberculous lesions elsewhere.

The *external genitalia* are sometimes affected, lupous-like nodules of a bluish color, prone to ulceration, being formed about the labia and introitus. The *vagina* is relatively very resistant, and lesions there are practically always in association with others of the uterus and tubes. There may be isolated tubercle nodules scattered in the mucosa, or, as in a case described by Davidsohn, a tuberculous granulation tissue thickly flecked with caseous areas may line the canal. In the *uterus* itself the mucosa of the body is by far more commonly affected than that of the cervix or portio vaginalis. The lesions may be in the form of discrete nodules in the mucosa, but more commonly there is a widespread destruction of the mucosa, which is converted into a thick, caseous layer, which extends deep into the muscle. Sometimes in case any obstruction to the cervical canal is present a quantity of necrotic and fluid material may accumulate in the cavity of the uterus, producing a sort of tuberculous pyometra. Tumor-like nodules of cauliflower-like form have been observed in the cervix and about the external os, sometimes giving rise to difficulty in diagnosis on account of their resemblance to carcinomatous growths. The *Fallopian tubes*, of all parts of the genital tract, are most commonly tuberculous. The usual lesion consists in great thickening and rigidity of the wall, with destruction of the whole mucosa and the caseation of the lining layer of tuberculous granulation tissue. The complete occlusion of the tubes by this material accounts for the almost invariable sterility of women with genital tuberculosis. Both in the tubes and uterus proliferative changes in the epithelium in course of development of the tuberculous lesions have been observed, and have greatly complicated the histological appearances.

The *ovaries* are less commonly tuberculous. When they are affected the lesion consists of caseous areas developed in the stroma and usually not connected with the follicles. Tuberculosis of cysts in the ovary has, however, been observed.

Extensive adhesions about the tuberculous pelvic structures and a tuberculous peritonitis are very common accompaniments of the condition. However, tuberculosis of the bladder and kidneys occurs in this connection by no means so frequently as in genital tuberculosis in males. This is easily understood on account of the less intimate anatomical association of the organs in the female.

As to the pathogenesis of the condition the question arises at once as to the mode of extension of the infectious agent. There are those who regard the direct infection of the vagina and uterine cavity by the use of infected instruments, etc., and by coitus with a tuberculous man as a prominent factor; but while such a possibility cannot be denied, the weight of evidence is not in favor of this view even in married women, to say nothing of virgins

and children, in whom the condition frequently occurs. Numerous efforts to produce tuberculosis of the uterus and tubes by the experimental inoculation of tubercle bacilli into the vagina of animals have sometimes succeeded, but Baumgarten, in a recent paper with Basso, claims that although tuberculosis of any portion of the genital tract may be produced by inoculation, an ascending genital tuberculosis does not occur. Tuberculosis of one tube or cornu does not infect the other, and extension is always in the direction of the stream of secretion. Hegar speaks of an ascending and a descending genital tuberculosis, explaining the ascending form as due to the transmission of the bacilli by the lymphatics in the para-vaginal and para-uterine connective tissue. The descending form, he thinks, may arise from the entrance of the bacilli into the fimbriated end of the tubes from a peritoneal tuberculosis or even from intestinal ulcers from which the bacilli have reached the peritoneum. Most authors, however, raise objections to the idea that tuberculosis of the tube may be secondary to tuberculous peritonitis, since the peritonitis is usually less advanced than the tuberculosis of the tube, and very often is entirely lacking.

The bacilli may be carried to these organs by the blood stream from an older focus elsewhere, and this idea is the most widely accepted. Why the tubes should be most frequently the seat of the lesion and show more extensive changes than the rest of the tract is not clear, but it may perhaps be regarded as a specially favorable tissue for the growth of the bacillus.

**Tuberculosis of Various Glands.—Breast.**—The breast was formerly thought to be immune from tuberculosis, but is now known to be affected not infrequently. Several possible paths for the entrance of the bacilli into the tissue have been pointed out, of which the blood stream and efferent ducts are perhaps most important. Cases have been reported in which caries of the ribs or a tuberculous pleurisy have by extension given rise to the infection, and others have believed that in cases in which the axillary glands were swollen and caseous the infection may have travelled backward along the lymphatics from those glands. It seems more probable, however, that the tuberculosis of the axillary glands may have been in those cases, as in so many others, secondary to the tuberculosis of the breast. The disease has not been observed in children before puberty. It occurs chiefly in women, but has been seen in men. It may affect all ages, but is much favored in its development by pregnancy and lactation, and most frequently affects women in the prime of life.

The lesions are found in the form of discrete, caseous nodules, usually in the interstitial tissues, or as large, abscess-like areas in which the semifluid content has resulted from the destruction of a great deal of tissue. The tubercle formation and caseation are exactly as elsewhere. The acini are encroached upon and gradually grown through and obliterated. Similarly the lumen of the ducts may become occluded. Such rather small nodules may run a slow course and be healed, at any rate in part, and it is on that account that tuberculosis of the breast is so often overlooked. The larger tuberculous lesions cause the breaking down of acini and interacinar tissue, and may sometimes produce sinuses which extend to and through the skin. Such changes have been frequently described under the name of "cold abscess."

**Spleen.**—Tuberculosis of the spleen, notwithstanding that there have been descriptions in the literature of a primary affection, may be regarded as

always secondary to tuberculous lesions of other organs and the mode of entry of the organisms is doubtless always by the blood stream. In practically all cases of disseminated tuberculosis tubercles in the spleen are found. These may be miliary, but it is well recognized that such lesions tend to reach a relatively great size in the spleen as compared with the liver and various other organs. Such conglomerated tubercles rapidly undergo caseation and stand out prominently against the surrounding dark-red pulp as rounded, opaque, yellow masses. In one specimen the caseous tubercles reached a diameter of 2 cm., and were quite sharply outlined by a gray, fibrous capsule. Most often they are small and extremely numerous, projecting from the splenic pulp as gray or opaque, yellow nodules. Their histological character is the same as in other tissues. As they are usually associated with an acute splenic tumor, they give rise to a considerable enlargement of the spleen, and in the cases of so-called primary splenic tuberculosis this enlargement has been especially conspicuous and has led to the idea that the spleen was the first tissue to be affected.

**Thyroid Glands.**—The thyroid, long held to be almost immune from tuberculosis, has been shown in recent years to possess no such complete immunity, although it is true that tuberculous lesions of the thyroid are uncommon, primary tuberculosis of this gland being especially rare. In autopsies on tuberculous individuals Chiari has found in 100 cases 7, Fränkel in 50 cases 5, Simmonds in 100 cases 3, and Hegar in 1563 cases 57 cases of tuberculosis of the thyroid. It appears usually in the form of scattered miliary tubercles in the course of an acute general miliary tuberculosis, but sometimes as a localized tuberculosis with caseous nodules. These have in general the character of such lesions as seen elsewhere, and may, as in Peterson's case, reach considerable size. They are generally poor in tubercle bacilli. Tomellini has recently made a minute study of the pathogenesis of tuberculous lesions in this gland experimentally produced by injection of bacilli into the carotid in rabbits, and finds that they develop essentially as in other tissues. He concludes that the thyroid exhibits no special immunity in this infection.

Roger and Garnier and other more recent writers, including de Quervain and his student Sarbach, have emphasized the occurrence of a general sclerosis of the thyroid in cases of tuberculosis in which there are no actual tuberculous lesions of the gland itself. This injury to the epithelium and resulting sclerosis are held to be the effect of the action of diffusible toxins produced by the tubercle bacilli in the affected lungs or elsewhere. No symptoms have been noted in any of these cases, but Carnot and Delion have recently reported a case of tuberculosis of the lungs with tetany and death in convulsions, in which they found caseous lesions of the parathyroid glands at autopsy.

**Adrenal Glands.**—The adrenal glands show no such relative freedom from tuberculous lesions, but are frequently affected, scattered miliary tubercles being perhaps less often described than larger, caseous areas, which produce great destructive changes. Isolated tuberculosis of the adrenals has been described several times, probably as the result of some inconspicuous primary lesions, but it forms, as a rule, part of a more generalized affection. The caseous areas appear as opaque, yellow patches in the enlarged gland, involving both cortex and medulla, and not infrequently including the associated sympathetic nerve structures. In some cases there is an attempt at encapsulation, and very large masses of necrotic material may extend beyond the

normal limits of the gland, surrounded by fibrous tissue, their relations being recognizable only by the persistence of small portions of the gland substance. In other cases the tuberculous lesion may be shrunken to a small, scarred, calcified area, buried in adhesions with surrounding organs.

Interest in tuberculosis of the adrenals depends chiefly upon the symptom-complex of Addison's disease so frequently associated with it. It is quite true that any other change which destroys the adrenals gradually will bring about this disease, and, further, that there are many cases of tuberculosis of the adrenals in which a great part of the gland is destroyed without any such symptoms; so that it is really not known which of the various constituents of the gland are responsible for the symptoms. Apparently their appearance in characteristic form depends upon the gradual destruction of the gland, and de Vecchi has reproduced them by the injection of tubercle bacilli into the gland, which by their destructive influence gradually converted the glands into caseous material. Extirpation of one gland is without effect, but extirpation of both leads to the death of the animal within a very few days, or even hours, with symptoms of an intense intoxication. Couzin has described an acute form of Addison's disease which is fatal within a few days, and which is without the well-known bronzing of the skin, but shows the intense toxic and nervous symptoms. Evidently this is dependent upon the more rapid destruction of the glands by the tuberculous process, which, as Couzin shows, prevents the normal neutralization of a poison which he thinks is produced by the activity of the muscles, and which then appears in the blood. The theory of Wiesel that the appearance of these symptoms depends upon the destruction of the whole chromaffine system, which is constituted by cells in the sympathetic ganglia and in the medulla of the adrenal, while the cortex of the adrenal is not concerned is tempting, and goes far to clear up the inconsistencies of various cases, but his observations have not yet been widely confirmed, and are disputed by Karakascheff.

**Tuberculosis of the Central Nervous System.**—While cases of tuberculous affection of the brain and meninges are of rather common occurrence, they form a relatively small proportion of all cases of tuberculosis. Only on the supposition that some hidden tuberculous lesions elsewhere have been overlooked, or by the possibility of transmission of tubercle bacilli through the ethmoid plate of the nose, can such lesions be thought of as primary or unconnected with other tuberculous disease in the body. In the great majority of cases the primary affection is found in tuberculosis of the lungs.

**Brain.**—The most common form of tuberculosis of the brain is that which affects chiefly the meningeal covering, the pia of the base of the brain being the portion which usually shows the most extensive alteration. Nevertheless, the tubercles there are very often associated with others in various parts of the brain. It is thought that the tubercle bacilli are brought there by the blood stream, and Hektoen traces the development of the tubercles from the inner walls of the bloodvessels; they soon affect, however, the whole tissue of the meninges, and there is usually to be found, on examination of such a brain, a thick, yellow, opaque exudate over the basal portion covering the pons, the medulla, and the optic chiasm, and extending in the sulci along the course of the vessels toward the upper surface of the brain. Close inspection will reveal small, gray nodules embedded in this exudate, and arranged along the course of the bloodvessels. These are often especially clearly seen on pulling aside

the temporal lobe and examining the vessels in the Sylvian fissure. These lesions, which are accompanied by hyperæmia of the tissues, usually fade away to a great degree as one passes toward the surface of the cerebral hemispheres, and over the spinal cord they are also usually less intense.

Microscopically, one finds in those cases which have developed very rapidly a considerable percentage of polymorphonuclear leukocytes in the exudate, but usually it is composed chiefly of polyblastic cells of various forms, all members of the series being found, from the numerous small cells to the very large, actively phagocytic cells with large, vesicular nucleus and abundant protoplasm. The bloodvessels are especially affected, their walls being eccentrically thickened by masses of new-formed tissue of tubercle-like structure, which have developed chiefly in the adventitial coat; less advanced new formation of tissue is evident in the intimal coat, the media being passively encroached upon from both sides. This mass of epithelioid cells, usually without definite giant cells, is very prone to caseation with fragmentation of the nuclei, and hence the opacity of many of the nodules seen along the vessels. Partial or complete obliteration of the affected vessels is not uncommon.

Similar changes are frequently found in the *ependyma of the ventricles*, where definite minute tubercles often appear which are visible as tiny grains upon the choroid plexuses and are not to be confused, as Ophüls has pointed out, with the minute, dense nodules found in the same position in ependymitis granularis, which occurs with various chronic diseases. As seen in some cases, these minute tubercles have clearly the structure of tubercles, and tubercle bacilli have been demonstrated in them. They are often accompanied by an abundant exudate of fluid, with wandering cells and fibrin, which produces the internal hydrocephalus, thought by some writers to be so characteristic of tuberculous meningitis. The amount of fluid varies greatly, but in most cases is not great. Tuberculous meningitis is frequently associated with allied lesions of the brain itself, when the condition may best be described as tuberculous meningo-encephalitis. These changes in the brain consist in the presence of caseous tubercles in the brain substance, usually just under the meninges and continuous with the tubercles in the meninges, but they may be deeply embedded in the tissue of the brain. In general, such tubercles are relatively large and appear as rounded, yellow areas of opacity surrounded by a zone of red. As a rule, there are but few of these, and careful sectioning of the brain must be made to discover all of them. Sometimes, and then often without any associated meningitis, there may be but one or two such caseous masses. These solitary tubercles may reach a great size, and in two cases seen recently there were tumor-like structures of the size of a hen's egg occupying the greater portion of the cerebellum, leading to symptoms of ataxia. Composed chiefly of caseous material, the margins of these masses exhibited beautiful tubercles with giant cells, partly obliterated tuberculous bloodvessels, and tubercle bacilli. Such large tubercles are sometimes seen in the spinal cord, where they cause great disturbances by interrupting the nerve tracts. The nerve roots are also sometimes involved, and in a recent case extensive paralysis of the lower portion of the body was due to the invasion and destruction of nerve roots by tubercles developed within the dura.

Tuberculous lesions of the *dura* are usually produced by extension from caseous areas in adjacent bones, and are, as a rule, localized in that neighborhood.

**Tuberculosis of the Bones and Joints.**—In all instances except in those in which the skeletal structures are encroached upon by tuberculous processes arising in adjacent tissues the bacilli must be brought to them by the blood stream, and it is practically certain that such bacilli come from some primary lesion which may be so small as to be overlooked or may be healed when the osseous lesions have developed.

Such osseous lesions arise very frequently in young children, but are by no means uncommon in more advanced age. They affect most frequently the short bones in which cancellous tissue is abundant, such, for example, as the vertebræ, the carpal and tarsal bones, and the epiphyseal portions of the long bones, while the diaphysis of these latter and the bones of the skull are less commonly their point of origin.

Beginning in the cancellous bone as grayish-red, translucent infiltration, the process soon extends with the formation of many tubercles and a tuberculous granulation tissue among the marrow spaces. This is usually associated with both rarefaction and eburnation or induration of the bony material, the inflammatory process promoting in places the excessive new formation of the bone, while the neighboring bony trabeculæ are eroded and thinned out. Caseation follows, often with the complete destruction of the affected area, sometimes with sequestration of the indurated part. A cavity is formed filled with soft, yellow, caseous material, often containing fragments of necrotic bone. Exceptionally such a focus may heal spontaneously, but usually it advances either toward the diaphysis of the bone or more commonly toward the articular surface and the joint. In early life the destruction of the epiphyseal cartilage by such disease may seriously limit the growth of the bone, but probably more important is the limitation of growth and actual atrophy which results from the inactivity of the limb.

Extension of the tuberculous process into a joint is followed by different results, according to the rapidity of advance. If the joint be invaded while in its normal general condition a dissemination of bacilli throughout its cavity usually results, and the development of an exudate of serofibrinous character, which may then be absorbed and followed by the growth of a tuberculous granulation tissue over the synovial surface. This may in time become very thick and translucent, and is often accompanied by a great accumulation of fluid, and by marked œdema or fibrous induration of the tissues about the joint (*e. g.*, the so-called white swelling of the knee), or without much or any exudation of fluid the tuberculous granulation tissue may rapidly undergo caseation and erosion. The cartilage of the joint is entirely passive and may be lifted up and dislodged over a caseous focus in the bone, or may undergo a softening with loss of its elasticity, so that it in some cases becomes actually "smeary" in consistence and is soon destroyed by the apposed ends of the bones. In such cases the exposed and partly caseous bony ends are often crushed into one another and extensive deformity is produced. Often before the caseous focus in the bone reaches the joint, the synovial cavity has become obliterated in part or completely by inflammatory adhesions, so that there is no longer a question of a synovitis, but the tuberculous process continues to extend from one epiphysis to the next.

Other cases progress much more slowly and there is time for extensive new formation of tissue in and about the joint, not only in the form of exostoses which often limit the mobility, but also in thickenings and villous outgrowths from the synovial membrane itself. Degenerative and mechanical com-

pression of the fibrinoid synovial outgrowths produce in some cases the pedunculated or free corpora oryzoidea, or rice bodies, which are smooth and of about the size and form of a melon seed. Tubercle bacilli have been demonstrated in them. In other instances the so-called lipoma arborescens results from the great overgrowth of the tissue of the joint, producing polypoid branched structures sometimes several centimeters in length. These are composed largely of fat, but usually contain tubercles. Usually, the active destructive processes in the joints, leading to the loss of the synovial membrane and the cartilage and the erosion and crushing of the ends of the bones, are not confined to those tissues, but the adjacent structures become involved, and not only is there œdema and cellular infiltration and induration of those tissues, but sinuses and fistulæ are formed which burrow along the fasciæ, often to a great distance, until they reach the skin. A bluish, abscess-like swelling shows itself for a time, and finally opens to give drainage through the tortuous channel to the caseous debris from the bone and joint.

Extensive collapse and displacement of the bones may occur in the rapidly progressing cases, so that, for example, while the head of the femur remains fixed in the acetabulum, the caseous neck breaks and the trochanteric end of the femur becomes dislocated to a point high upon the pelvis, with great shortening of the leg. This destruction is perhaps most frequently seen in the vertebræ, where caseous areas develop usually first under the anterior ligament, producing a prevertebral abscess, but quickly extend to soften and destroy the cancellous bone. This allows of the collapse of the centrum, with the angular deformity of the spine; when only one centrum is affected the spinous projection in the back is a sharp one; if a number of vertebræ are destroyed there is produced a rounded kyphosis. From such a vertebra with its prevertebral abscess similar sinuses are often seen to burrow their way down through or beneath the psoas muscles until they can appear at the skin in the groin or on the inner side of the thigh—the so-called psoas abscesses.

*Periosteal* tuberculosis, as, for example, in the ribs and other bones which lie near the skin, may give rise to quite large accumulations of exudate and caseous material, which have long been known as cold abscesses.

As to the pathogenesis of the bone and joint lesions of a tuberculous nature it may be said that in many cases it is impossible from the advanced stage of the disease to tell whether bone or joint was first affected. König maintains that the synovial cavity is always first infected, but Guillemin and many others hold the opposite view and support it by statistics, which show that in the majority of cases the adjacent focus in the bone gives rise by its extension to the infection of the joint.

**Tuberculosis of the Muscles, Tendons, and Fasciæ.**—The muscles, tendons, and fasciæ are generally involved in tuberculous processes as the result of extension of the lesion from an adjacent caseous area in bones or elsewhere, but cases have been described in which isolated hæmatogenous foci were found embedded in the muscle. The lesion produces cavities in the muscle filled with a soft, caseous material, and lined with a tuberculous granulation tissue with giant cells of the usual character. The muscle fibers in the immediate vicinity are in large part atrophic, but some are greatly enlarged. Various French authors, among whom Hemery may be mentioned, distinguish three forms: the cold abscess of muscle, disseminated tuberculous myositis, and tuberculous muscular sclerosis.

**Bursæ.**—Isolated tuberculosis of bursæ may also occur, but are usually a sequence of tuberculosis of adjacent bones and joints. Schuchardt describes three forms of tendon-sheath tuberculosis which closely resemble those seen in joints, namely, tuberculous fungus of the sheath, in which the lining is covered with a tuberculous granulation tissue, a nodular form in which a persistent, tumor-like, gray, non-caseating mass is formed, and finally the rice-body hygroma analogous to the similar change in the joints.

**Tuberculosis of the Skin.**—Much confusion still seems to exist in the classification of tuberculous lesions of the skin, and there are several affections the tuberculous nature of which is still a matter of doubt. Distinctly tuberculous are those forms known under the names lupus, scrofuloderma, tuberculosis ulcerosa, and tuberculosis verrucosa cutis, to which Kaposi has recently added another group with the designation tuberculosis miliaris cutis. Besides these there are certain affections, such as lichen scrofulosorum and lupus erythematosus, which frequently occur in association with tuberculosis, but the strictly tuberculous nature of which is not yet decided.

Lupus, which by some authors (Unna) is divided into circumscribed and diffuse forms, is an affection of the skin produced by infection from without, and not necessarily associated with tuberculosis of the internal organs or underlying tissues. The lesions occur either in the form of pale brownish or bluish, non-vascularized nodules, sharply marked off from the adjacent normal skin, or as spreading hyperæmic areas elevated above the surrounding surface, and showing their brown pigmentation only when the bloodvessels are emptied by pressure. All possible transitions between these forms occur with various modifications produced by the excessive growth of the epidermis, etc. They appear usually upon the exposed surfaces of the body, as, for example, in the skin over the nose and cheeks. The course of development is usually slow, and the lesions are extraordinarily persistent, reappearing often after they had apparently undergone healing. Ulceration is frequent, with extensive destruction of the tissue and subsequent scarring, which proceeds sometimes to such a degree as to cause the most unsightly deformities of the face.

Histologically, these nodules are composed of tubercles quite similar to those seen elsewhere, developed in the skin sometimes in the form of compact, non-vascularized nodules, at other times as a sort of vascular granulation tissue studded with tubercles. Tubercle bacilli can be demonstrated in this tissue, which proceeds to caseation, and in that way to the formation of ulcers in the skin. The localized nature of the disease may often be shown by the possibility of bringing about healing.

The term scrofuloderma is applied to those tuberculous lesions of the skin which are directly produced by underlying tuberculous foci in bones, joints, lymph glands, and other tissues. Such are the changes described above as resulting from the extension of sinuses from tuberculous foci in bone to the skin. They appear at first as soft, fluctuant elevations of bluish-red color, which finally break down and, liberating a quantity of caseous material, remain permanently open. Such deep cavities are lined with an abundant tuberculous granulation tissue, the caseation and ulceration of which often extends widely to the neighboring skin. This, as is evident from the description, is a lesion of the skin of distinctly secondary nature. The third form, tuberculosis ulcerosa, is less common, and appears in individuals suffering from severe visceral tuberculosis as ragged, superficial ulcers in the mouth

and adjacent skin, about the external genitalia, etc., evidently due to an autoinoculation of the skin.

Rather different in character from these is the verrucose form of the disease, which is due to direct infection of the hands, in most cases from contact with tuberculous materials. The nodules are often spoken of as necrogenic tubercles, or "Leichentuberkeln," on this account. Appearing as nodules covered by a much thickened and keratinized epidermis, and formed in the depths of the skin of an infiltrated connective tissue with tubercles, these areas often tend to heal spontaneously. They are in many instances later associated with widespread internal tuberculosis, but on the whole they present a mild form of the cutaneous tuberculous affection. They cannot be very sharply separated in any classification from the cases of lupus.

The miliary form of tuberculosis of the skin which Kaposi has recently emphasized has been long known as a part of a generalized miliary tuberculosis occurring in the form of multiple, scattered nodules of a tuberculous nature in the skin, and tending to caseation and ulceration.

As to the affections mentioned above, which are frequently associated with tuberculosis of the internal organs, it may be said that while it cannot in most cases be demonstrated that lichen scrofulosorum and lupus erythematosus are anatomically tuberculous in nature, it is thought by many that they may be the expression of the effect of the toxins of the tubercle bacillus upon the skin (Hallopeau).

Jacobi, Riehl, and others have demonstrated tubercle-like structures in cases of lichen scrofulosorum with giant cells, but these are not typically tuberculous, and the bacilli have not been definitely demonstrated; inoculations were negative. Interesting, although not conclusive, evidence in favor of their tuberculous relations is found in the fact that they react to tuberculin injections in much the same way as the lupous nodules. Practically the same doubts exist as to lupus erythematosus, and Jadassohn is forced in respect to it, as in the case of lichen scrofulosorum, to leave the question undecided after considering the evidence on both sides.

# CHAPTER IX.

## THE SYMPTOMS OF TUBERCULOSIS.

By LAWRASON BROWN, M.D.

In a chronic disease, whose average duration is at least three or four years, symptoms command for long periods the attention of both patient and physician. Their importance in diagnosis has for some time been recognized, but their relation to immediate prognosis, that is, whether the patient is improving or failing, has not been so clearly stated. The value of recording symptoms accurately has not been sufficiently emphasized. In some cases pulmonary tuberculosis is almost entirely a disease of symptoms; in others, it is true, of physical signs, but these are far in the minority.

The symptoms can be grouped in two classes: first, the general, and second, the localizing symptoms. The general symptoms are often not sharply defined and may be so slight as to escape the patient's notice. They are of less importance in localizing but of more importance in determining the presence of the disease. The relative importance of these symptoms is difficult to determine, but none is of greater value to the physician than fever.

**Fever.**—This is characterized by chronicity, postmeridian occurrence (often following a subnormal morning temperature), occurrence in attacks, which may supervene upon a normal or slightly elevated temperature and often by slight constitutional disturbance. The maximum and minimum temperatures, although variable in height and duration, usually occur at the same times each day in any individual patient. The presence of fever, when not due to complications, indicates that the disease is active. Fever may precede all other symptoms. Few patients are apyretic throughout the entire course, but in no other chronic disease with elevation of bodily temperature are the constitutional symptoms of fever so often lacking. In fact the slight discomfort caused by the fever may be said to be its most striking characteristic. It is not unusual to find a patient up and about and fairly comfortable whose temperature is 102° every afternoon, and some patients even feel stimulated when their temperature rises. Most incipient cases are, however, afebrile as soon as their life is well regulated.

It is of the greatest importance to know the temperature of each patient. He should be provided with a good thermometer recently tested, and a little care in teaching him how to take his temperature is invaluable. If taken by mouth, in cold weather he should be in a warm room for ten to thirty minutes with his lips closed. If taken by rectum, it is wise not to take the temperature soon after a stool, and care must be used to avoid fæces in inserting the thermometer. Menstruation and pelvic inflammation may affect the rectal more than the oral temperature. Rise of temperature is usually perceptible earlier by rectal than by oral measurement. Without doubt

the rectal temperature is more accurate and less subject to minor variations. It is always important to determine roughly the variation between the mouth and rectal temperatures for each patient, and when once determined it can be taken by mouth only, which many prefer. Some even in this case take both temperatures morning and evening and only the oral during the day. In patients with fever the difference is always most marked for the lower temperatures and least for the higher.

The temperature should be taken every two hours, beginning on awakening, until the medical adviser is fully acquainted with the range. Then if the temperature be normal it may be taken on waking, at the time when the daily maximum occurs, and at 8 P.M. The morning temperature should always be taken before the toilet is begun. Much individualization is necessary when patients take their own temperatures. In neurotic patients much tact must be employed; frequently the thermometer must be discarded to overcome "thermometer fever," and as little attention as is consistent with proper treatment should be paid to the temperature. This consists, in afebrile patients, of taking the temperature for two days every two to four weeks, and during the interval if there is the slightest suspicion of fever. If the patient cannot sleep or has headache he should take his temperature during the night, as in some cases the rise occurs at night only, or a second rise may occur at that time.

*The "normal" temperature* varies slightly for individuals and considerably with rest, exercise, and time of day. The individual variation, while slight for the rectal temperature, is more pronounced for the oral. During rest in bed the rectal temperature may be said to be normal when it varies between 97.3° and 98.5° on awakening, 98.6° and 99.1° in the forenoon, and 99.1° and 99.5° in the afternoon. In some cases, however, it may reach nearly 100°. The oral temperature rarely sinks below 97° in the morning and seldom goes above 99.2° in the afternoon or evening. The temperature when the patient is exercising, and especially just following exercise, is higher and less certain. Exercise affects the rectal temperature much more than the oral. Simply getting out of bed in the morning may raise the rectal temperature some tenths of a degree, and after exercise a rectal temperature of 101° has been frequently recorded in apparently normal individuals. A rectal temperature of 100.4° immediately after exercise is not to be considered abnormal. The oral temperature rarely shows much elevation after exercise and may be lowered for some time on account of the cooling influence of the more rapidly respired air. Tuberculous patients even with a normal temperature at rest show after exercise a much greater rise (by rectum) than normal persons (Penzoldt's phenomenon). Fat anæmic individuals may have elevation of temperature, especially after exercise. In old age the normal temperature is lower than in adult life, while in childhood the range is much greater.

**Cause of Fever.**—This is primarily the effect upon the heat centre of the tuberculous toxin or protein, absorbed from the tuberculous focus, rendered no doubt more irritable by previous absorption of the same irritant in doses too small to cause fever. The fever produced by the injection of tuberculin proves that secondary organisms and their products are not necessarily its cause. The fever late in the disease, the hectic or absorption fever, is due in part at least to the absorption of bacterial proteins other than those produced by the tubercle bacillus and to the absorption of the

necrotic matter from the softening tissue or pneumonic processes. Some hold that the tubercle bacillus produces a second toxin which can lower the temperature and that the labile temperature in the tuberculous is due to the action of these two toxins.

The temperature curve with its daily rise or rises can be readily explained by the effect of bodily exercise upon absorption. The absence of fever after the long rest at night is thus explained as well as the afternoon rise after the exertion of the morning. No doubt this explains also the rise of temperature at night in some patients, with severe cough on lying down. Absorption, therefore, plays an important part, and the higher fever in acute tuberculosis or in acute attacks is due to the greater absorption through the more patent lymph channels (Cornet). It has long been recognized that the disease in patients with fibroid phthisis or with chronic cavity formation may be afebrile, although advancing. In other cases fever occurs only when the outlet of the cavity is plugged or when fresh areas with patent lymph channels are involved. Fever caused by overexertion may not occur for several days.

**Fever in Chronic Pulmonary Tuberculosis.**—Every known type of fever may occur, but the usual temperature curve is one which is normal or slightly subnormal in the morning and rises to 99.5° or 100° (by mouth) between noon and 9 P.M. The fastigium lasts usually for two or three hours, but may be so short that it is recorded only when the temperature is taken every two hours. As a rule, the maximum is between 3 and 5 P.M., the minimum between 2 and 4 A.M. Many patients have a slight rise for months before their attention is called to it by some other symptom. As the disease advances the febrile attacks are sharper and in some instances more protracted, but the acute exacerbations of fever are often of ten to fourteen days' duration, the time which is required in experimental tuberculosis for the formation of agglutinins.

In still more advanced stages, fever is present at some time every day, and may be continuous, intermittent, or, as is more usual, remittent. Several minor oscillations may be present each day, or the temperature may fall to normal for a day or two a week. The temperature seldom exceeds 104°, but is frequently subnormal. A fall of temperature is often observed after the formation of a cavity. In many cases, however, the temperature goes from normal or slightly below to 100° or 101° with great regularity. The division of tuberculous fever into fever of tuberculization, of ulceration, and of absorption cannot be maintained, as in general all three processes occur simultaneously.

It must not be expected that the temperature curve will always follow the course just outlined, undisturbed by other causes. Complications, tuberculous and non-tuberculous, as well as an advance of the tuberculous process in the lungs, may cause fever. A sudden and sharp rise of temperature without warning rarely occurs in the ordinary progression of the disease.

The temperature of the tuberculous patient is very unstable, due in part at least to the effect of the tuberculous toxin upon the nervous system, especially upon the heat regulating centre. Slight mental excitement or slight physical exercise causes more rapid heart action and increased stimulation of the heat centre, either from the increased toxin in the blood or from an increased amount of toxin in contact with the heat centre. However this may be, the tuberculous invalid is prone to rise of temperature from

trivial causes, as well as from bronchopneumonia, acute gastritis or enteritis, influenza, and almost any intercurrent disease. The rise of temperature in 50 to 60 per cent. of patients from one to seven days before or during the menstrual period and the "digestion fever" said to occur in some patients, usually anæmic, after the chief meal of the day, are due, no doubt, to this lability of the temperature.

Rise of temperature, if of any duration and not due to complications, indicates activity in the pulmonary lesion. The disease, however, can progress without discoverable rise of temperature, although this takes place usually only when the individual has no longer sufficient powers of resistance. As a rule, the degree of activity can be told from the temperature chart. Even slight rise of the minimum temperature is to be regarded as suspicious of increased tuberculous involvement, while the maximum temperature usually shows the intensity of the disease or the activity of the secondary organisms. If the minimum temperature is normal or nearly so and the maximum 100.5° to 101.5°, and seldom above, a slow disintegration with an absorption of the inflammatory products is more likely than an advancement of the disease (Saugman). High intermitting fever indicates a severe and deep-seated lesion and often quick destruction of tissue. Fever may occur and the patient show all signs of increased activity, but several days may elapse before any increase in the physical signs becomes evident. In fact, some patients recover from the febrile attack before the lesion causing it is discovered. A rise to 106° or 108°, if present at all, usually occurs shortly before death, but in the writer's experience it is much more common for the temperature which has been high to fall below normal for a day or two before death. Hæmoptysis, repeated at intervals for several days, is usually accompanied by a slight rise in temperature. When an extension of the tuberculous process or an aspiration pneumonia follows hæmoptysis the temperature usually becomes high and continuous. In a few cases the temperature falls after hæmoptysis when the amount of blood lost is not large. The temperature on the two sides of the body may vary and is highest usually on the side affected. The face and ear are frequently more flushed on the affected side.

**Fever in Acute Pulmonary Tuberculosis.**—In these cases fever is usually a marked symptom and may closely simulate that of typhoid fever or pneumonia. In rare instances it suggests malaria, a diagnosis far from uncommon in pulmonary tuberculosis. The temperature curve, however, seldom closely simulates a single tertian infection. In a few cases the rise extends over a period of two days to become normal on the third. This may be repeated a number of times. In most cases of acute tuberculosis the temperature is continuously high, with but slight morning remissions.

In acute miliary tuberculosis, either primary or secondary, the temperature is usually high, continuous, with very slight morning remissions, and may range between 102° and 105° for days. Marked remissions with a normal temperature of several days' duration may occur. The "inverse" type of temperature is rarely observed either in this or other forms of pulmonary tuberculosis. Its occurrence usually indicates that the temperature rises during the night and does not fall until 6 to 9 A.M. If a two-hour chart is kept throughout the night it is more frequently noticed, especially in subacute or chronic cases. It has been observed in only three or four patients at the Adirondack Cottage Sanitarium, and then but for a short period. It

is said to be the only temperature curve due solely to pulmonary tuberculosis.

In acute pneumonic tuberculosis the temperature curve is at times similar to that of typhoid fever in the second week, or pneumonia, but more often it resembles typhoid in the third or fourth week, with more or less marked remissions. The temperature usually ranges from 100° or 101° to 103° or 104°.

Fibroid tuberculosis may occur with slight or no elevation of temperature, or the temperature may be subnormal. High intermittent fever, often very irregular, suggests, in early stages of the disease, tuberculous enteritis, salpingitis, etc.

Some affirm that the presence of mixed infections can be told from the temperature and that the "streptococcic" curve is characteristic. This curve, due no doubt in part to secondary organisms, shows marked vacillations. In the morning the temperature is often markedly subnormal, and Lebert records one case in which it reached 89°. In the afternoon or evening the temperature rises rapidly to from 101° to 104°. A variation of 4° or 5° is frequent, and as much as 14° has been observed. Mixed infection cannot be diagnosed from the temperature curve, although Koch has stated that a temperature over 100.4° is due to secondary infection. In patients with a favorable prognosis, *e. g.*, in those at the Adirondack Cottage Sanitarium, the temperature rarely fell below 95° (91° lowest recorded) and rarely exceeded 105° (106° highest recorded). In 123 of these patients whose temperature reached 102° or over, 43 per cent. did not go above 102°, 26 per cent. reached 103°, 29 per cent. 104°, and 2 per cent. 105°. The greatest recorded variation in twenty-four hours was 10°. Uncomplicated tuberculosis of the serous membranes may produce a hectic fever.

**Weight.—Loss and Gain.**—Wasting has long been recognized as the symptom most characteristic of pulmonary tuberculosis, popularly termed for this reason "consumption" or "phthisis." It is the result of the disease, stands usually in direct relation to the stage and chronicity, and is not a conservative process as some affirm (Pollock). This wasting affects all the organs of the body except the liver, which may undergo a fatty change, and possibly the bones. The fatty and muscular tissues are most affected. Loss of weight may be the most prominent and in a few cases the only symptom. It may occur so gradually that it escapes attention for some time, or it may be very rapid in the early as well as in the later stages. The scales, with the thermometer, give usually the most reliable information concerning the progress of the patient, but those with slowly advancing disease may lose little or no weight. This is no doubt due to individual resistance, but may depend upon the low virulence of the tubercle bacilli present. A slight loss usually occurs during menstruation, but is quickly regained. Loss of weight is in proportion to the duration of the disease and young patients lose more rapidly than older.

The "normal" weight of patients with pulmonary tuberculosis is about ten pounds less on an average than what they should weigh. The bearing of this fact upon diagnosis is readily seen and should be given more regard in life insurance work than the occurrence of pulmonary tuberculosis in some member of the family with whom the patient has never come in contact.

The cause of loss of weight is best explained as the effect of the toxin absorbed from the pulmonary lesion upon cell nutrition in general. Hays

recognizes this as the primary cause of the loss of weight, which is due directly to the increased metabolism caused by the fever and also to a deficiency of the digestive ferments. Later, the adaption of the organism (more digestive fluids of an inferior quality) to the changed condition would, he holds, prevent loss and further gain. In any case the digestive organs are often early affected, producing defective assimilation, loss of appetite, vomiting, and consequent emaciation. Loss of weight is not dependent upon fever, as it may occur in the absence of this symptom, but usually they go hand in hand, the weight increasing as the fever decreases. The loss of weight occasioned by nervous excitement and exercise can be explained by the increased absorption of toxin. Forced muscular exercise is nearly always followed by loss of weight. Intercurrent diseases and complications, *e. g.*, diabetes mellitus and influenza, may cause a rapid and considerable loss of weight. Montenegro has observed, when a closed becomes an open lesion, a replacement of loss of weight by a slight gain.

Loss of weight in chronic disease may amount to one-third to two-fifths of the previous weight. If a patient lose one-fourth of his normal theoretical weight his nutrition is apt to be considerably disturbed and a loss of one-third is a grave omen. Patients with extensive œdema may be up and about and a considerable loss of weight (ten or twelve pounds) may easily escape detection. A larger percentage of weight can be lost by fat individuals. Great emaciation is rarely present in acute disease. The greatest loss recorded is 130 pounds in a man weighing 271 pounds in health. A loss of 5 or 6 pounds a week is not unusual for a short time.

**Gain in Weight.**—This depends not upon ingestion, but upon assimilation. One patient may eat little and gain and another eat an enormous quantity and lose. Patients who are so fond of meat that little else is eaten are less likely to gain than good general eaters. Some foods seem to have especial influence upon gain in weight, *e. g.*, eggs, milk, cream, and cod-liver or olive oil. Many patients who have had high fever gain in weight when the fever decreases, although a continuously elevated temperature may still be present. Antipyretics are of value when they decrease afternoon fever and enable the patient to eat. Patients with fever need an amount of food greater than normal to maintain their weight, and when kept out-of-doors they frequently digest enormous amounts of food well.

Gain in weight, if much loss has occurred, is practically a necessity for improvement and may occur at any stage. Gain usually occurs as soon as the life of a patient is properly regulated. Change of climate is not so essential in the case of the poor as good hygienic conditions. For the well-to-do, who have looked upon these conditions as necessities and always enjoyed them, change of climate, at least at first, is often necessary to stimulate nutrition and gain in weight. Many patients in advanced stages gain in weight for three or four months after a change of climate, but then gradually lose.

*Cold* seems to have a marked influence upon weight-gaining in the healthy as well as in the tuberculous. The weight curve in pulmonary tuberculosis, if not influenced by change of climate or other factors, rises from August to Christmas (sometimes to November), remains more or less stationary with minor fluctuations from Christmas to Easter (March), and sinks gradually from Easter to August. This corresponds closely with the normal weight curve and is based upon a study of the weight charts of 1200 patients at the

Adirondack Cottage Sanitarium. Gabrilowitch, at Halila, has found that patients gain more in the very short days in winter than in the longer, warmer, and sunnier summer days. Berger, however, has failed to note this. Great dryness in itself is not conducive to gain in weight. The effect of exercise upon gain in weight is at times striking. Some patients at rest gain little, but put upon carefully regulated exercise begin to gain at once.

The average gain in weight under treatment depends upon whether or not forced feeding is employed, the activity of the symptoms, and the amount of weight that has been lost. Patients with far-advanced disease and considerable loss of weight usually gain more on an average when the disease becomes quiescent than those with advanced but less than those with incipient disease. A study of 164 patients at the Adirondack Cottage Sanitarium who had gained 20 pounds or more (average 21.6 pounds) shows that these patients do better as a rule, but a large gain of weight does not assure cure. Of these patients, the 22 who have died gained on an average 28½ pounds, 2 pounds more than those who have remained well. The largest gain in weight that has come under the writer's notice occurred in a man with a cavity, rather extensive disease on one side, and a slight affection of the opposite apex. Returning to his work against advice, his weight fell from 145 to 115, and his lung condition became worse. During a second sojourn of two years his weight increased to 215 pounds. Men as a rule lose more weight and gain less than women.

The average gain in weight of 901 patients at the Adirondack Cottage Sanitarium was 14 pounds. In 2 patients, in early stages, without much loss of weight, gains occurred respectively of 15 pounds in fifteen days and 27 pounds in twenty-eight days. A gain of 2 pounds a week is satisfactory. Weight may be gained irregularly, *i. e.*, a gain may occur on the first and third days and a loss on the second. The mental condition directly affects the weight. The gain in weight in many cases occurs first on the chest and face.

The *persistence of the gain in weight* is often remarkable. In some cases (about one-third, Berger) the gain is continued when the patient returns to his home and lives properly. Weight gained during exercise is more permanent than weight gained at rest. Weight acquired through a liberal use of milk and eggs, especially if without exercise, is often quickly lost. The explanation of this rests less upon the hypothesis of Dobell, that "the stability of the fats of the animal body in resisting too rapid oxidation is dependent upon the degree of solidity which they possess at the temperature of the living animal at any given time," than upon the fact that such observations are usually made in advanced stages, when patients have lost much weight and would quickly lose any weight gained, even if the ingestion of "material capable of supplying the adipose tissue with solid fat" was the cause of the temporary gain.

**Metabolic Changes.—Proteid and Fat.**—The emaciation is due to a toxin absorbed from the seat of disease, which, while it acts upon the nervous system, causes also directly a loss of appetite and so prevents repair of the normal waste of the body. Late in the disease, vomiting and diarrhœa act in the same way. This weakens the resistance and so favors extension of the disease. The increased amount of toxin thus produced acts directly upon the cellular protoplasm, which in time loses its power of regeneration. When the toxin is absorbed in sufficient quantities fever is produced, which in turn affects the metabolism. The body fat is little affected until later.

when dyspnœa, chills, and other pronounced symptoms occur. For these reasons May holds that the severest toxic action and the most lively tissue destruction are seen in caseous pulmonary tuberculosis.

**Inorganic Salts.**—Changes also occur in the excretion of other organic and inorganic substances. Calcium phosphate as well as lecithin and nuclein are increased, and Mitulesku finds the phosphorous output parallel with the nitrogenous. Magnesium and calcium salts are increased in the terminal stages, especially when fever and loss of appetite are present (Ott). The "demineralization" of the French observers is not peculiar to tuberculosis, but occurs first and irregularly in later stages. Ferrier holds that phosphaturia and tuberculosis are closely related. Decalcification, he believes, is of much importance, and should be vigorously combated. This work still lacks sufficient confirmation.

The excretion of ammonia and of indican, especially in intestinal complications as well as when cavities become septic, is increased. The different phenols and skatols are also increased in destructive processes. Urobilin is increased usually, but in very acute processes is decreased.

**Respiratory Exchange.**—The gaseous exchange in the lungs, in spite of marked destructive processes, undergoes practically no alteration. Robin and Binet have asserted that more oxygen is absorbed and more $CO_2$ excreted than in health (increase of pulmonary ventilation 80 per cent. and over), and advance this as a means of diagnosis. This work has failed to be confirmed by many observers.

**Loss of Strength.**—This often occurs as the primary manifestation, but is rarely recognized as such at the time. Many patients begin early to tire easily, and work which once was a pleasure begins to drag. This debility may be present to a very marked degree and out of all proportion to the extent of the discoverable lesion. A point often mentioned by the patient is that while he seems to have as much muscular power as ever for a single act, he is incapable of sustaining for any length of time muscular or, in some cases, mental work. His endurance is considerably lessened. The muscular tonicity has been found to be greatly diminished in the incipient stage, even when the muscular power and nutrition are good. The loss of strength is most probably due to the effect of the disease upon the nervous system.

As the disease progresses and, in fact, often within a few weeks after the patient has "given in," he feels much better. Loss of strength is of course directly proportional to the general condition. Nothing is more deceptive than the robust appearance of many patients undergoing the modern treatment compared with their lack of strength. The slow return of strength is a most striking feature in many cases and one of no inconsiderable importance in treatment. In far-advanced cases the debility may become extreme, and yet, on the other hand, it is remarkable what many patients, seemingly tottering on the brink of the grave, can accomplish. Stevenson fully recognized this in *Aes Triplex* and in his own life.

**Night-sweats.**—These, while rare in the early stages, occur more frequently in pulmonary tuberculosis than in any other disease. In a few cases they precede all other symptoms and even physical signs. This, however, is rare, as they are usually associated with fever and a subnormal morning temperature. As the disease progresses, or during acute attacks, the night-sweats become more frequent, and in the later stages drenching sweats are common, and may occur not only at night, but whenever the patient falls

asleep (sleep-sweats). The sweating, so exhausting, so unpleasant, and so depressing that the patient dreads going to sleep, usually occurs early in the morning and possibly not until during a nap following the morning cough.

The sweats vary much in severity. At times so slight as to be scarcely perceptible, they may be so profuse that the night robes have to be changed three or four times a night and possibly some of the bedding as well. Sweats were absent in 10 per cent. of Louis' cases and in 41 per cent. of 2344 cases at the Phipps Institute, Philadelphia. Sudamina, more frequent in acute, rarely occur in chronic cases following sweats. Acute inflammatory processes and diarrhœa may hold the sweats in abeyance for a time. They are less frequent in children, and in patients with diabetes mellitus. Hemidrosis may occur, but is accidental. The night-sweats are general when severe, but the slighter forms are often more localized, and occur most frequently about the head and neck or extremities. The sweat has been found in some cases to give a tuberculin reaction on injection, but never contains tubercle bacilli. No record of the amount of sweat has been published, but in some cases it exceeds twenty ounces.

**Cause.**—The sweat glands are under the control of centres which can stimulate or inhibit the secretion. Increased blood supply to the skin increases secretion of sweat, and consequently these glands are closely connected with the vasomotor centre. Early in pulmonary tuberculosis, sweating is usually the result of poisoning of the sweat, vasomotor, and heat centres by the tuberculous toxin; in the more advanced stage the sweat may be the result of fever, which stimulates the sweat centres, the vasomotor centres (causing dilatation), and the glands; and late in the disease the sweat centres or glands may be stimulated independently of the heat and vasomotor centres by the toxins of the secondary organisms as well as by those of the tubercle bacillus.

The increased frequency of sweating in acute processes is due probably to the more rapid absorption of toxins. Some hold that overstimulation of the vasomotor (constrictor) centre finally gives way during sleep to a greater relaxation than normal. The increased blood supply then causes the sweat. The presence of the toxin, however, is not always sufficient to cause sweating, and some pathological changes in the circulation and nutrition are generally necessary. The absorption of necrotic matter or pus is, according to some, the chief cause. In most cases the sweat glands respond to slighter stimuli than normally. The connection of sweating with rise and fall of temperature some think is direct, while others hold both due to the same cause. Bradycardia, weakness, and anæmia have been suggested as causes, but in some cases are lacking. Lessened respiratory surface, and therefore lessened secretion of moisture and $CO_2$, with stimulation of the sweat centres, has also been advanced as an explanation, but this would only explain sweats in the late stages.

**Chills.**—These may occur early in the disease, and when present daily often give rise to a diagnosis of malaria. They occur usually before, seldom after, the rise of temperature. Slight shivering, blueness of the nails, or gooseskin are early signs of fever. Following a sweat, chills are not infrequent. Complications are sometimes ushered in with chills.

**Blood.**—The blood picture varies with the stage, the acuteness, and the complications. In patients with incipient disease it is often normal, and during treatment the erythrocytes and the percentage of hæmoglobin

are frequently above normal. Other patients are anæmic from the outset. The earliest and most constant change is the reduction of the color index, and chlorosis in many instances is masked tuberculosis. A slight diminution of the erythrocytes is frequent in this group of cases, while the leukocytes may be either slightly increased, decreased, or, as is more usual, normal. When the disease reaches the advanced stage, the pallor of the face, which may be present earlier, becomes often very marked, and is at times in strong contrast with the red color of the lips and mucous membranes. The blood here is often normal in every particular, and the erythrocyte count and hæmoglobin may be above normal. The leukocytes are usually very slightly if at all increased. The explanation of this lies in the concentration of the blood and a real leukopenia. The large amount of fluid lost by the increased salivary and bronchial secretions, the night-sweats, and diarrhœa if present, and probably also the action of the tuberculous toxin producing an increased flow of lymph to the tissues, are all factors. In far-advanced cases, when secondary infection has taken place, the blood presents usually the same conditions that occur in toxæmia.

**Erythrocytes.**—These may be as low as 1,000,000 to the c.mm., but they rarely fall under 3,000,000 in uncomplicated cases. Counts of 6,000,000 in patients undergoing treatment are not uncommon. Fever, unless it is septic, has no effect upon the erythrocytes. In general a diminution of the red cells is the dominant characteristic. Many degenerative changes have been described, but none seem to be characteristic. Shortly after hæmoptysis the blood shows a slight reduction of erythrocytes (counts of 1,000,000 or even 360,000, however, have been made), and a transitory leukocytosis, present only in some cases and proportional to the severity of the hæmoptysis. Nucleated red cells are rarely found. The hygienic-dietetic treatment produces a marked increase in the amount of blood as well as an increase of the erythrocytes and percentage of hæmoglobin in patients who are improving.

The erythrocytes in 155 patients at the Adirondack Cottage Sanitarium (elevation 1600 ft.) taken on admission to the institution (some patients, however, having been under treatment for several months) gave the following figures:

| | Male. | | Female. | |
|---|---|---|---|---|
| Erythrocytes. | Incipient. | Advanced. | Incipient. | Advanced. |
| 4,000,000–4,500,000 | 2 | 0 | 1 | 1 |
| 4,500,000–5,000,000 | 6 | 3 | 16 | 4 |
| 5,000,000–5,500,000 | 13 | 17 | 6 | 15 |
| 5,500,000–6,000,000 | 9 | 9 | 6 | 8 |
| 6,000,000–6,500,000 | 4 | 1 | 3 | 1 |
| 6,500,000–7,000,000 | 7 | 5 | 2 | 2 |
| 7,000,000–7,500,000 | 1 | 3 | 3 | 2 |
| 7,500,000–8,000,000 | 1 | 3 | 0 | 1 |
| Total | 43 | 41 | 37 | 34 |
| Average | 5,618,605 | 5,831,171 | 5,386,216 | 5,529,941 |

**Hæmoglobin.**—Many patients under treatment or with advanced disease show a percentage considerably above normal. With progression of the disease the percentage usually falls and may reach a low figure. The hæmoglobin in this series was estimated usually by the Tallquist scale, but in a few cases the von Fleischl apparatus was used. The results in 154 cases are as follows:

| Hæmoglobin. | Male. | | Female. | |
|---|---|---|---|---|
| | Incipient. | Advanced. | Incipient. | Advanced. |
| 65–69 per cent. | .. | .. | 1 | .. |
| 70–74 " | .. | .. | 1 | .. |
| 75–79 " | 2 | 2 | 0 | 2 |
| 80–84 " | 2 | 3 | 5 | 1 |
| 85–89 " | 8 | 4 | 11 | 5 |
| 90–94 " | 16 | 18 | 11 | 18 |
| 95–99 " | 9 | 11 | 4 | 5 |
| 100 " | 6 | 2 | 4 | 3 |
| Total | 43 | 40 | 37 | 34 |
| Average | 91.0% | 90.4% | 88.2% | 90.3% |

The spectroscopic examination of the oxyhæmoglobin shows similar results. In a majority of all cases the color index is reduced.

**Leukocytes.**—These are at times somewhat reduced in number, and it is possible that the cause of the leukopenia may act in a similar way to reduce the leukocytosis usual in some of the complicating diseases. Counts of 3000 to 5000 are frequent in incipient stages. In advanced stages 10,000 to 12,000 are not unusual, and in a few cases, late in the disease, the leukocytes may even be higher. In acute miliary tuberculosis of the lungs, leukopenia is more often present than leukocytosis. The latter is at times present in caseous pneumonia. In chronic fibroid conditions leukocytosis is usually absent unless a cavity is present. Tuberculous complications, unless accompanied by secondary infection, rarely produce much increase in the leukocytes. During softening a leukocytosis is usually present and it may occur with tuberculous hyperplasia of the glands with slight destructive pulmonary changes. Leukocytosis is said to be a constant accompaniment of cavity formation, and a prolonged absence of leukocytosis is held to exclude this condition. Such, however, is not always the case, especially in chronic cavities (Ewing). Acute tuberculosis supervening upon a leukæmia may reduce markedly the number of leukocytes, but chronic pulmonary tuberculosis and leukæmia may coexist without reduction in the number of leukocytes.

The differential count shows considerable variation. The polymorphonuclear cells vary between 60 and 95 per cent., but are usually about 80 to 84 per cent. Leukocytosis in pulmonary tuberculosis is almost always due to increase of these cells. Recent work upon the cellular elements of serous effusions has drawn much attention to the large number of mononuclear cells. It seems, however, to be more constant in pleuritic effusion than in the blood either of these or of other patients with chronic pulmonary tuberculosis. Some have tried to show a prognostic value for this type of leukocytosis, believing a low mononuclear count decidedly less favorable than a higher one. In low counts the large and small lymphocytes are usually relatively and possibly absolutely increased. Myelocytes may be present, but mastzellen rarely occur. Much interest was aroused by Teichmüller's observation on the eosinophiles in the sputum in favorable cases. However this may be, as the disease advances some hold the number of the eosinophiles in the blood decreases, and as it retrogrades the number increases, but Ullom and Craig question this. The leukocytes counted in 155 cases at the Adirondack Cottage Sanitarium, before breakfast, while fasting, gave the following results:

| Leukocytes. | Male. | | Female. | |
|---|---|---|---|---|
| | Incipient. | Advanced. | Incipient. | Advanced. |
| 4,000- 5,000 | .. | .. | 2 | .. |
| 5,000- 6,000 | 1 | 1 | 2 | 2 |
| 6,000- 7,000 | 6 | 4 | 5 | 3 |
| 7,000- 8,000 | 5 | 8 | 12 | 3 |
| 8,000- 9,000 | 8 | 4 | 6 | 7 |
| 9,000-10,000 | 6 | 7 | 1 | 4 |
| 10,000-11,000 | 3 | 8 | 2 | 5 |
| 11,000-12,000 | 4 | 2 | 1 | 4 |
| 12,000-13,000 | 2 | 2 | 3 | 3 |
| 13,000-14,000 | 3 | 1 | 3 | |
| 14,000-15,000 | 2 | 1 | .. | 1 |
| 15,000-16,000 | 1 | 2 | .. | 1 |
| 16,000-17,000 | 1 | 1 | | |
| 17,000-18,000 | .. | .. | .. | 1 |
| 18,000-19,000 | 1 | | | |
| Total | 43 | 41 | 37 | 34 |
| Average | 9950 | 9637 | 8485 | 9744 |

The blood platelets are normal or increased. Even in the most advanced stages their number is not reduced.

Arneth, from a study of the polymorphonuclear leukocytes, found that in health 5 per cent. contained a single nucleus, 35 per cent. two nuclei, 42 per cent. three, 17 per cent. four, and 2 per cent. five nuclei. Other observers have found in health a considerably larger percentage of cells with one nucleus, and more cells with two nuclei. In pulmonary tuberculosis the number of cells with fewer nuclei was much increased. Iodophilia is of little value in pulmonary tuberculosis.

The blood serum seems to possess a more or less specific agglutinating power for the tubercle bacilli. Maragliano's work shows that the serum of tuberculous patients with toxæmic symptoms has a toxic effect upon healthy and tuberculous animals, which resembles tuberculin poisoning.

The *bacteriology of the blood* has been frequently investigated with very contradictory results. That tubercle bacilli occur in the blood cannot be questioned and some recent work would seem to prove that more exact methods will yield more positive results. Up to this time, however, tubercle bacilli have rarely been found in the blood except in acute conditions, in the preagonal stage, and at postmortem. Inoscopy (Jousset) and the use of leeches (Gary) seem to aid materially in the search. The positive results obtained for other organisms are more numerous, but many have been questioned. Faulty technique would no doubt account for some, but there remain a number of cases in which other organisms have been recovered. The results in hectic patients have not upheld the theory of septicæmia, as in most cases the blood was apparently sterile. The tubercle bacilli are said to be more frequent in blood from the spleen, and some have unwisely suggested aspiration of the spleen for diagnostic purposes.

The *dry residue* of the blood is lessened and the specific gravity lowered. Cellulose (glycogen) and calcium phosphate may occur. Fibrin is increased at first and decreased in the last stages. With the course of the disease the iron and potassium salts and phosphates decrease; the sodium salts increase. The reaction of the blood is more weakly alkaline than normally.

**Circulation.—The Pulse.**—The frequency and tension are early and often permanently changed. The size of the pulse, its fulness and regularity,

bear less definite relation to the pulmonary disease than the frequency and tension, and often until the late stages are only slightly if at all abnormal. The radial pulse is said to be influenced by the position of the arm on the affected side when contraction of the apex has occurred, and Foss has found a paradoxical pulse in 61 per cent. of 120 patients, while Sorgo noted a weaker pulse on the affected side in 8 per cent. of 397 patients.

*Frequency.*—Until thermometry was introduced this was the most important single phenomenon in the disease. Unquestionably it is nearly as important as the temperature, and in many cases is far more accurate for prognosis. The pulmonary patient borders constantly upon the verge of excitement, and the visit of the physician or a call at his office will often increase the pulse twenty beats a minute. The best record is that taken at the patient's home by a nurse to whom he is accustomed. This instability of the pulse has some connection with the decrease of blood pressure and a paresis of the vessels. Altitude increases the pulse rate somewhat, which may decrease in a short time or persist.

Increased frequency is often a striking feature and is of great value in diagnosis, as it stands most often in direct relation to the activity and extent of the disease and strength of the patient. The majority of all patients have at first a slightly increased rate (90 to 100), even when apyretic, and frequently when at rest in bed. The pulse rate and temperature may be independent, but more usually there is a rather close connection between the two, which some have tried to express by allowing ten beats for each degree of fever. An increase above this rate, they think, is due to cardiac weakness. Forced feeding may produce slight acceleration of the pulse for a time. In some cases the pulse shows increased rapidity for short periods, but this is rather unusual, as when it once becomes rapid it usually remains so for some time. Mental excitement, slight physical exercise, attacks of coughing, and a full meal have a strong tendency to increase the rate in early as well as in advanced cases. In the latter, however, the pulse tends to be constantly rapid, and, varying somewhat with the temperature, increases slightly every afternoon. The range is usually between 88 and 120. This tachycardia is seldom noticed by the patient. Often as he improves and after the temperature has become normal the pulse rate gradually decreases, but it may quickly fall to normal and remain so. Slight tachycardia may persist in healed pulmonary tuberculosis.

The *cause* of the increased frequency is still unsettled. It has been attributed to pressure upon the vagus by enlarged tracheobronchial lymph nodes, an explanation which certainly does not suffice in many cases. Brehmer thought the underdevelopment of the heart and the overdevelopment of the lungs were important factors. Another view is that it is due to the increased work thrown upon the heart by a narrowing of the lumen of the pulmonary vessels, or to a narrowing of the air passages, which Marié found diminished the number of respirations and accelerated the heart. A neuritis of the vagus, the fall in blood pressure, irritation of the sympathetic, increased irritability of the cardiac ganglia or muscle fibers, myocarditis, anæmia, and dyspepsia have all been suggested as factors. The most probable cause, especially in incipient stages, is a weakening of the cardiac muscle and its nervous control due to the tuberculous toxin, but this hardly explains the persistent tachycardia in some healed patients. Valvular disease of the heart in pulmonary tuberculosis exerts little influence upon the pulse rate.

**Blood Pressure.**—In many cases this is lowered from the very outset, and some have held that hypotension is present in the predisposed. A much greater variation exists between the blood pressure in a reclining and in an upright position than in health. Potain believes that this hypotension can be used to differentiate a true chlorosis from the secondary anæmia of tuberculosis. The hypotension is held by many to be due to the tuberculin, which undoubtedly lowers tension (Teissier). As the disease advances and pronounced constitutional symptoms occur, the blood pressure becomes less and 90 mm. of Hg. (Riva-Rocci manometer, with 9 in. cuff) is not uncommon. When complicated by emphysema, nephritis, arteriosclerosis, diabetes (Teissier), or cardiac hypertrophy the blood pressure may be raised.

**Heart.**—The heart may show little change throughout the entire course. It has long been held that it is reduced in size, and upon this Brehmer founded one part of his plan of treatment, graded walks. More recent observations have shown that hypertrophy is only a little less frequent than atrophy, which usually occurs only in cachectic patients. In 70 necropsies at the Phipps Institute the heart was normal in size in 32, enlarged in 26, and decreased in size in 12. Many complications produce an hypertrophy, so that it is difficult to draw any conclusions at autopsy in regard to the heart early in the disease. The orthodiagraph has, it seems, shown a slight atrophy in incipient and hypertrophy or dilatation in far advanced stages.

Displacement of the heart usually occurs gradually, but in some patients transposition to the right side seems to take place within a few days. The shrinking of the right lung frequently increases the area of pulsation and may so displace the heart that the pulsation is limited entirely to the right side, extending in some cases beyond the midclavicular line. Retraction of the left lung may cause cardiac symptoms varying from slight discomfort to pseudo-anginal attacks.

Murmurs are not uncommon either at the apex or base, but in the writer's experience are more frequent at the apex and usually systolic. Some occur in patients in whom anæmia can be excluded, where the displacement of the heart, if any, is slight, and where we are led to explain the murmur as due to pressure upon the great vessels. These patients show no cardiac hypertrophy. In a few patients murmurs occur in the interscapular region. Consolidation may transmit these murmurs widely. A cavity near the heart may alter the sounds, and murmurs synchronous with the systole are not infrequent in these cases. Murmurs are at times produced in cavities by the systolic distention of a large vessel or of an aneurism.

Acute dilatation of the right ventricle occurs far less frequently in tuberculosis than in other pulmonary diseases. In many chronic cases, where the intrapulmonary vessels are either obliterated or reduced in size, accentuation of the second pulmonic sound occurs and the shock is at times easily palpable. Over the second left intercostal space the second sounds are at times reduplicated (best heard when the patient reclines). A weakened first sound is rather frequent in well-advanced stages, and is often more pronounced during acute attacks.

Dilatation of the right side of the heart in advanced stages is, however, more frequent than many observers have held. Norris states that dilatation or hypertrophy of the right side occurred in 27 per cent. of 2344 patients in advanced stages, and in 21 per cent. of 143 autopsies. Accentuation of the second pulmonic sound occurred in 35 per cent., accentuation of the second

aortic sound in 18 per cent., and reduplication of the second sound in 40 per cent. of 2344 patients, hypertrophy or dilatation of the left heart in 2.6 per cent., tachycardia (pulse rate over 120 at first visit) in 17 per cent., bradycardia (pulse rate below 65 at first visit) in 1.5 per cent., and displacement of the heart in 1.7 per cent.

**Palpitation.**—This in neurotic subjects is usually a vexious phenomenon associated with hypotension. The slighter forms are frequent and few patients entirely escape them. The severe forms occur occasionally after too vigorous exercise, and are most likely to be met with in advanced stages. They are more frequent at puberty and at the menopause, sometimes precede hæmoptysis and accompany dyspepsia. Some have acute pain in the neck along the vagus. When a patient complains of palpitation the lungs should always be examined. Cardiac distress may also be found in a few patients not suffering from palpitation.

**Vessels.**—Pulsation in the cervical vessels is of frequent occurrence. Temporary dilatation of the subclavian artery has been described by West, who thinks it not rare. Dilatation of the veins upon the upper thorax and above and above the costal margin is quite common. A murmur over the subclavian artery, first described by Stokes, is not unusual under the outer third of the clavicle, and has been held to be of diagnostic importance. It is more common on the left side and is rare in women. It may appear or increase during inspiration or expiration, and is due either to anæmia or to overpression of the vessel by a thickening of the pleura or by a muscle. The murmur is not constant, is usually soft and blowing, and the position of the arm or pressure by the stethoscope may increase or produce it. Œdema of the lower extremities is rare except in the very late stages, when it almost invariably indicates great cardiac weakness.

**Cyanosis.**—This may persist for years while the patient enjoys comparative health. In many it is more pronounced in the morning. In the late stages the lips and nails become blue and the face and extremities are often swollen. In early stages it seldom occurs except as the result of severe paroxysms of cardiac excitation.

**Skin.**—The skin undergoes changes produced by malnutrition. In many patients in early stages, even in those undergoing treatment, the skin is pale, moist and chilly in every particular. The chilliness and cold sensations in feet are less frequent now than formerly. In the majority some pallor of the skin is present and often the vessels are well seen through the "semi-clear" and translucent tuberculous tissues. In some the skin is dry and coarse and the epidermis exfoliates in furfuraceous flakes. In late stages the skin is often dry and harsh, and even the mucous membranes become involved. This occurs most frequently on the trunk and extremities, and the skin feels like parchment and tears like paper. The sebaceous as well as the sweat-glands may be seen plainly and the skin becomes oily. A pungent odor from the sweat is often noticed.

Pigmentation occurs rather infrequently and may consist in a general browning of the skin, less marked than in Addison's disease, or in a patchy, dirty yellow or dark brown, more sharply circumscribed, which may occur on the face or trunk, the seat of irritation or inoculation. A connection between pigmentation and disease of the adrenal and lymph glands has been suggested, as the color of the skin is said to be more common when the latter organs are involved. Leucoderma is rare. Atrophy of the sebaceous

ally present, and, while usually accidental, may at times be due to a tuberculous toxin. It occurs in connection with acute conditions and adenitis, and in some appears only when the fever is at a maximum. It may closely resemble the rash of scarlet fever, but usually spares the mucous membranes. Petechiæ rarely occur. Purpura is seldom met with except in acute miliary tuberculosis, but some think it is occasionally due to the tuberculous toxins. Œdema of the skin rarely occurs except in complications or late in the disease. The hectic flush in late stages or a reddening of one cheek and ear in moderately advanced patients is common. Subcutaneous emphysema, with crackling on palpation, due to a rupture of the lung, is a rare complication. Local tubercle may develop on the hand. Herpes labialis occurs periodically with slight gastric disturbances in some patients, and is not uncommon after a tuberculin reaction.

*Hyperæsthesia* of the skin is common and is often elicited on percussion. It is rarely noticed below the third rib, is said to spread or contract with the advancement or retrogression of the disease, and to be more acute when the temperature is elevated. In lesions of the upper lobe it is most frequently present in the supraspinous fossa.

**Hair.**—The nutrition of the hair suffers especially during fever. It often becomes dry and lanky, and may split. The hair may come out in considerable quantities, but the alopecia is seldom patchy, partial, or complete. Premature grayness occurs accidentally, but may be due to poor nutrition. The arcus senilis may also occur early. In children and young persons the body is sometimes covered with a growth of fine, downy hair (Kidd).

**Nails.**—The down-curving of the nails may occur without, although usually with, clubbing of the fingers (Hippocratic digits), and is thought to be due to the loss of fat on the palmar surface and malnutrition of the matrix, as well as circulatory disturbances. It is said to occur more frequently in women, and is most usual between ten and thirty years of age. The ridges and furrows which occasionally occur are also due to poor nutrition.

**Alimentary System.**—Symptoms referable to the alimentary tract are present sooner or later in nearly every patient, and while not as frequent as symptoms referable to the respiratory system, rank second in importance to none.

**Gums.**—The gums in advanced cases, owing to the poor nutrition, are often spongy and soft, and pyorrhœa is not infrequent. A red line on the gums, first described by Fredericq in 1851, and pictured by Thompson, is not peculiar to pulmonary tuberculosis, but occurs in many wasting diseases and in some healthy persons. The cause of this bluish-red line is undoubtedly a mild gingivitis. Bleeding of the gums is very common and in streaky hæmoptysis should always be excluded. Caries of the teeth is frequent, due possibly to the gingivitis, and is of great importance on account of the necessity of thorough mastication. Thirst is rarely great unless diabetes mellitus or fever is present or unless the patient breathes through the mouth.

**Tongue.**—The condition of the tongue varies directly with the condition of the patient. In incipient cases with good digestion it is clean, moist, and normal, as also in many advanced cases. When gastric complications occur or when the patient sleeps with an open mouth, the tongue is usually covered with a white fur, which may become dark from food or medicine. In advanced stages sordes or a deeply fissured tongue may be present.

**Tonsils.**—The tonsils may be hypertrophied, but adenoid tissue is rarely present. Chronic granular pharyngitis is common. Stomatitis is infrequent in early cases, but aphthous ulcers occur at all stages. Salivation or stoppage of Wharton's duct, with œdema of the mouth, tongue, and neck, is rare and probably accidental. Thrush may occur on the soft and hard palate, tonsils, tip and root of the tongue, and mucous membranes of the cheeks. Usually of slight importance, it may penetrate into the deeper vessels, cause thrombosis, and even produce cerebral metastasis.

**Digestion.**—The digestion may be good to the end and many patients recover without the slightest digestive disturbance. A majority, however, suffer at some time from digestive disorders (70 to 90 per cent.), and women more than men. The type of the disease seems to exert less influence than its acuteness. Patients who escape have usually been good eaters, and the appetite is the best guide to the digestion. Alcoholics and those who have abused their digestion pay usually heavy penalties. Distress or anorexia may occur while apparently all the gastric functions are normal, but on the whole the gastric tolerance is remarkable and the amount of food consumed by some patients, even while at rest, is truly astonishing. In many patients with gastric disturbance no pathological changes in the stomach, except possibly slight hyperæmia, have been found. Dyspepsia when present usually becomes less marked as the pulmonary disease advances, and when it is arrested the dyspepsia generally subsides.

The gastric juice is normal in many early cases (50 per cent., Brieger), but as the disease advances it is frequently abnormal, and in severe cases over 80 per cent. (Brieger) show some change. Hyperacidity may be present in early stages, while later subacidity is more common. The weakly alkaline sputum must be swallowed in large quantities to produce any effect by neutralization upon the gastric acidity. The secretion of HCl is independent of the fever, but with other constituents of the gastric juice seems to be reduced in far-advanced stages. The digesting power of the gastric juice has been found to be reduced in some cases.

The motor functions of the stomach usually run parallel with the condition of the muscles in general, and accordingly the motility may be deficient in advanced but also in some early cases. With loss of motility, dilatation of the stomach occurs.

The rapidity of absorption is little changed at first, but with dilatation and loss of motility it is much diminished. Gastroptosis in these cases is occasionally present.

The *gastric disorders* have been well studied by Marfan, who, under the "usual dyspepsia of phthisis," discusses the variable modes of onset and its frequent termination by gastritis. The appetite usually fails and after meals some distress is noticed, varying from slight distention to actual pain or cramps. Eructations are not uncommon, but pyrosis is infrequent. The gastric mucosa is very irritable and in some cases eating is followed by cough and cough by vomiting without nausea. This occurs more frequently after the evening meal, as the morning cough has in most cases completely cleared the air passages. The vomitus in these cases usually consists of undigested food. A peculiarity of the vomiting thus produced is the fact that the patient is often able and willing to eat again at once. In these cases the motility of the stomach and the digestive power of the gastric juice may be lessened. Such changes are probably purely functional and not connected with the

fever. Lasègne has remarked that a patient who eats and digests well while having fever is a "phthisiker."

This dyspepsia may first call the attention of the patient to his health or it may develop at any stage. It is often preceded by hyperacidity and its accompanying symptoms, and is caused by irritation of the peptic glands, by the tuberculous toxins or of the mucosa by swallowed sputum, or possibly is due to the anæmia. Disturbances of the nervous system may be the cause of slight digestive disorders. Hays holds that the early digestive disturbances are due to the altered gastric juice, and that the disappearance of the symptoms which often takes place later is due to an adaptation of the organism, namely, an increased secretion of gastric juice of lessened digestive power. Fenwick thinks that chemical alterations in the blood, occurring at the onset, are directly responsible for both the digestive disturbances and the anæmia.

The terminal gastritis is characterized by a furred tongue with red papillæ, an absolute anorexia, and a persistent diarrhœa. Besides these the other symptoms of the initial dyspepsia may all be present and exaggerated, and dilatation and motor insufficiency are constantly present. The abdomen is often sensitive, most markedly about the umbilicus.

*Anorexia.*—When tissue hunger is greatest, wrote Dettweiler, the appetite is often least. Anorexia, however, is rarely complete in the earlier stages unless profound constitutional symptoms are present. Many patients complain of no appetite, but eat, and eat well, and these are less liable to digestive disturbances. Again, many patients are hungry until they see the food or until a few mouthfuls are taken, then appetite may be replaced by nausea. The appetite is frequently capricious, good for one meal and lacking for several, or good one day and lacking for several, but on the whole it diminishes as the disease progresses. The tastes may undergo striking changes, and food once relished becomes repugnant and strange or bizarre articles of diet are craved. An antipathy to fats exists in some patients. Desire for food is at times closely connected with the temperature, and at noon or evening, whenever the maximum temperature occurs, the appetite is poor or lacking. This is not always the case, as many patients with high fever eat well. In a surprisingly large number the appetite remains good until shortly before death.

*Pain.*—Slight gastralgia is frequent in early as well as in late stages. Often it is fleeting and needs no treatment. In others the pain occurs regularly either immediately after eating or later, and is rarely the only symptom present. Distention is a frequent cause. Pain in the epigastrium, immediately after eating, may occur when the stomach is normal and ulceration is present in the transverse colon.

Gastric fermentation, due in many cases to overfeeding, is probably the most frequent of all gastric disturbances. The resulting distention may come on immediately after each meal, and varies from a feeling of fulness and discomfort to one of acute pain. In some cases it seems to vary with the temperature, and, beginning during the afternoon, reaches its crisis in the early evening.

*Nausea.*—Nausea is very common at all stages. It may occur for some time before the physical signs are sufficiently pronounced for diagnosis. In the terminal stages it is often present and accompanied by vomiting. Many times it is manifested only in the morning, and may prove most

stubborn. Again it comes on, when after one or two mouthfuls the appetite vanishes and the patient tries to force down a little more food. It often occurs without vomiting, and may cause much distress.

*Vomiting.*—This may occur with or without nausea. Without nausea it is usually due to violent paroxysms of cough, the emetic cough of Morton, and is more frequent in basal lesions. This vomiting usually takes place just after meals or when a change of posture is made, generally on arising. One patient with a large cavity in the upper lobe vomited every morning and never expectorated at any time. The vomiting in these cases is mechanical. Vomiting after nausea or other gastric symptoms is less frequent, but far from uncommon, especially in the later stages. In the first case the patient is often able to eat again at once; in the second the thought of food is repugnant. Other causes of vomiting are nervousness, pressure upon the vagus by bronchial glands, hyperæsthesia of the posterior pharyngeal wall (sputum furnishing the necessary irritation), and nasopharyngeal catarrh. Vomiting may precede all other symptoms and persist after the disease is arrested.

**Intestinal.**—The intestinal secretions and the peristalsis may undergo changes of varying intensity. Constipation, which is more frequent than diarrhœa except in the very last stages, is no doubt in part due to the milk diet, in part to lessened peristalsis, caused possibly by the weakened musculature. Whatever the cause, constipation and at times obstipation is most troublesome and needs careful attention. It may be present until death, notwithstanding severe intestinal ulceration.

*Diarrhœa.*—This may occur for months before a diagnosis is made. One patient who had coughed since Christmas, began in April to have infrequent (one or two a day) loose stools which lasted until August, when after a hæmoptysis tubercle bacilli were found in the sputum, which he ceased to swallow. Treatment had been of no avail, but from this time on his stools were normal. The swallowed sputum can in many cases set up a catarrhal enteritis, which is more marked by its chronicity than by the frequency or profuseness of the stools. This form is more frequent in women, but may be caused by sputum swallowed during sleep. The tuberculous toxins may cause diarrhœa by irritation of the sympathetic system and increased peristalsis, by catarrhal enteritis, or by superficial erosions (catarrhal ulcers). This would no doubt explain the diarrhœa which in rare cases follows tuberculin.

Many tuberculous patients have diarrhœa from apparently trifling causes. In some, milk or raw eggs will in the course of time produce a pronounced griping and diarrhœa. A chilling of the abdomen and slight indiscretion in diet, especially indigestion due to overfeeding, are sufficient in others. The cough and expectoration may diminish when the diarrhœa increases.

In any digestive disorder the stools should be examined for undigested food and for bacilli to exclude the swallowing of sputum.

**Liver.**—A fatty liver is said to be of frequent occurrence, due to the action of the tuberculous toxins on the liver cells. Possibly the large amount of food or alcohol previously taken may have some effect.

**Spleen.**—Enlargement is rare and occurs practically only in acute miliary tuberculosis or in acute exacerbations. Amyloid degeneration may occur.

**The Genito-urinary System.**—The genito-urinary organs present few symptoms in uncomplicated pulmonary tuberculosis.

**The Urine.**[1]—This is usually normal in every particular in early stages, but when fever is present it may be concentrated and deposit urates. The amount is often increased, especially at first, and the majority of patients arise one or more times at night. The liberal milk diet no doubt often accounts for this, but a true polyuria can occur. Some oliguria may be present in far-advanced cases. Robin has found the solid residue in 46 fatal cases to be about 30 gm., in 6 who failed 33, and in 21 who remained stationary or improved 51 gm. per diem. He considered a patient who excreted less than 30 gm. per diem as in the beginning of the cachectic stage. The urinary salts vary with the temperature and the stage of the disease. The chlorides may decrease in exacerbations or when profuse expectoration occurs, but are usually normal.

Phosphaturia is held by some to be an early indication of pulmonary tuberculosis (Powell). Calcium phosphate predominates and increases as the emaciation progresses. Both calcium and magnesium increase at first and later decrease. Croftan considers a high calcium content important in early diagnosis. Phenol has been found in the urine, especially just before death. Indican occurs more frequently, especially in children, than in health. It is of little or no value in diagnosis. The urea varies in amount, frequently normal at first and often decreasing late in the disease; it varies with the diet, exercise, and temperature. Acetone, sugar (without diabetes), peptone, and albumose have been found. Albuminuria is rare in early and is usually met with only in far-advanced stages. Teissier has described an intermittent form occurring in young individuals with a family history of pulmonary tuberculosis. The diazo reaction occurs inconstantly in some patients in advanced stages, who usually present marked symptoms, constitutional and local.

In 656 patients at the Phipps Institute, Philadelphia, for the most part in a far-advanced stage, sugar was present in 13, albumin in 153. Casts were noted in 37 and the diazo reaction in 60 among 495 cases. Poisonous substances, ptomains, have been found in the urine of patients with apparently normal kidneys, and it has been claimed, but not proved, that tubercle bacilli in the urine may be the only means of diagnosing an early pulmonary lesion. Flick and Walsh have found tubercle bacilli in the urine of patients with pulmonary tuberculosis in 73 per cent. of 60 cases (the differential diagnosis being based upon the use of alcohol and Gabbett's solution), while Supino was unable to recover them after very painstaking researches. In 14 out of 17 far-advanced patients inoculation experiments showed tubercle bacilli in the urine (Walsh). It is no proof that because injection of urine or its residue causes a "reaction" similar to that produced by tuberculin, tuberculin is in the urine, for other substances may cause this reaction.

Inflammation and displacement of the uterus, common in pulmonary tuberculosis, are probably caused by an aggravation of preëxisting trouble, and in some cases to cough.

**Menstruation.**—This may be scanty or cease early in the disease, especially when the patient is anæmic. Change of residence may also affect some patients. An onset at the time of puberty may delay menstruation for years. As the disease advances the menses usually, if not previously disturbed, become irregular and finally cease. With improvement menstruation begins

[1] See Clemens in Ott's *Chemical Pathology of Tuberculosis.*

again. In a few the menstrual function continues to the end. Menorrhagia occurs in a few cases, but rarely persists. It is a common tendency with women to attribute many exacerbations of the disease to the recurrence of the menstrual periods, and in some cases the symptoms are undoubtedly more pronounced at this time. The premenstrual fever occurring for about one week before menstruation is well recognized, while many hæmoptyses occur and recur at this time. The expectoration may be increased or present only during this period.

**Pregnancy.**—Pregnancy can occur in very advanced stages and one patient, failing gradually for months, became unconscious four days before term and died during delivery. During pregnancy the disease is often held in abeyance, to proceed more rapidly after parturition.

**The Nervous System.**—The nervous system is often early affected, and few patients entirely escape some nervous disturbance. This would be expected in neurotic individuals, but while usually more pronounced it is by no means confined to them. A tuberculous family taint is supposed to render the patient more liable to nervous disorders.

**Psychical Changes.**—An apparent change in the disposition of the patient is not infrequent. It is in many cases only "apparent," as in a large number the real character is laid bare. By many all sham and pretension are thrown aside, perhaps unwittingly, and selfish traits, previously fostered by foolish parents, may become so pronounced that the patients try to exert despotic sway over all their associates and attendants. They will not brook the slightest interference with their wishes, and, when opposed, either fall into a rage or burst into tears. Fortunately, these examples are rather rare. On the other hand, some dispositions, naturally quiet and refined, seem as the disease advances to become so unselfish, so ethereal that they suggest another sphere in more ways than one. Chronic invalidism rarely leaves the character unchanged, and treatment which constantly enforces self-consideration is not conducive to unselfishness. And yet years of institutional life, months spent in health resorts, and the constant solicitude of the family and friends affect singularly little the character of many chronic tuberculous patients.

The restraining influences of early training, of education, of vocation, of the manner of life, all seem to lapse in many patients, and sanatorium experience teaches that many act as if they were still school-children, looking upon physicians as boys do upon tutors or preceptors and endeavoring by many little ruses to gain their own way. A foolish act undetected they think can do no harm. The emotions, too, are less restrained, and unexplainable misunderstandings and differences may arise. Many cannot bear to hear of suffering, and in some, trifling causes produce tears. Emotional weakness is common. Jealousy, especially in women, is at times marked to a high degree.

Indecision, vacillation, and changeableness are frequent characteristics in some patients. Fancied grievances turn them against old friends. Their judgment of men and affairs, their plans and outlooks often change from day to day, or may be entirely reversed. Forced inactivity produces lack of concentration in some. Only the most exciting literature can arouse them. In others again every act is characterized by morbid haste and impulsiveness and, to use a familiar expression, the patient becomes a "bunch of nerves."

The mental faculties are generally well preserved to the end and, in fact, may become more acute and out of all proportion to the bodily strength.

The patient may plan and attempt to put into execution many schemes consigned to failure at the outset. He may endeavor to acquire a monopoly of the cottages in a health resort and sign many foolish contracts. Whatever he plans he must be about at once, little realizing the effect upon his jaded body. "Death catches him like an open pitfall, and in mid-career, laying out vast projects, and planning monstrous foundations, flushed with hope, and his mouth full of boastful language." In a few, ideas of self-importance and of grandeur, great nervous irritability, suspicion and susceptibility to suggestion are marked.

This, however, is not a true picture of the ordinary tuberculous patient. The vast majority, though depressed at first, soon rebound and improve or fail, they remain the same men and women they were before they became sick. They may be optimistic, pessimistic, sanguine, choleric, or phlegmatic. The *spes phthisica* is common and may be pronounced even to the end, but the vulgar opinion has been until recently so pessimistic that it is not possible for the patient to escape its influence, and many arguments are necessary to convince him of the possibility of a "cure." He quickly recognizes the serious illness of a fellow-patient, and it seems impossible that he should not realize the gravity of his case. Fortunately, these patients are little given to a frank discussion of their prospects, but when they can be led to discuss dispassionately their disease they often frankly acknowledge their despair. Familiarity luckily removes many stings, and he who faces death constantly often comes to face it fearlessly. The reverse is the case in some sad instances, and the physician is called to no harder trial than to listen to a dying consumptive pleading for life, which he cannot sustain.

**Neuroses.**—Neurasthenia is more common in pulmonary tuberculosis than in any other disease. No doubt it has an organic basis in the toxic poisoning of the higher centres, but, however that may be, few escape it. At first it may be so pronounced that it masks the tuberculosis, which may be overlooked for some time. In other cases it develops only when the patient is well on the road to recovery, and forms a serious complication. Physicians and nurses, when attacked, are peculiarly prone to this neurasthenia. Pressure in the head, giddiness, fear, anxiety, vasomotor disturbances, and especially sleeplessness are common. When pulmonary tuberculosis occurs in neurasthenia or hysteria the nervous symptoms are usually increased.

Hysteria occurs much less frequently and most often just before or during the menstrual period. It tends to disappear with the progress of the pulmonary disease, and is rarely seen in men. Aphonia is not uncommon, but convulsions or spasms are rare. In one patient a spasmodic contraction of the œsophagus permitted the swallowing of fluids only.

**Psychoses.**—Psychoses are very much rarer in pulmonary tuberculosis than pulmonary tuberculosis in psychoses. Two classes may be recognized: "first, a group peculiar to the disease itself; second, a group including the usual types of insanity determined by a lowering of nutrition" (McCarthy). In the first class are patients with no hope of recovery, but happy and contented and often with a decided grade of unreason. They closely simulate paresis. In 1674 cases of pulmonary tuberculosis, McCarthy found 4 patients, all with advanced disease, terminating fatally, but in whom a happy, contented state of mind existed, with expansive ideas and distinct delusions of grandeur. Their speech was paretic, and tremor of the tongue and hand

marked. This type of McCarthy's differs from the form described by Clouston, where depression advances to melancholia, and morbid suspicion, marked loss of memory, a desire to be alone, irritability, and delusions of persecution occur.

The second group includes melancholia, mania, dementia præcox, hysterical insanity, and delusional insanity. Melancholia develops in a few cases shortly after the diagnosis has been imparted to the patient, or it may occur in moderately advanced cases. In far-advanced cases it seems to be rare. Suicidal tendencies are not uncommon in these. Onset of the disease with mania is very uncommon, and later in the disease mania is also rare. The age incidence of pulmonary tuberculosis is the same as that of dementia præcox, and the association of the two diseases may be thus explained. Vertigo, cephalalgia, buzzing in the ears due to cerebral anæmia may occur, as well as hyperæmia, simple meningitis, pachymeningitis, and inflammation of the dura, with symptoms of hydrocephalus, especially in children, and toward the end somnolence and disturbance of consciousness, due, Ruehle holds, to cerebral œdema.

Tremors are common and usually occur on voluntary effort. They may persist after recovery, and no doubt in some cases existed previously to the onset of the pulmonary tuberculosis. The reflexes are often exaggerated, but may be decreased or absent, especially in marked asthenia. The knee-jerk is increased in one-half of the early cases. The ulnar reflex, a distinct wrinkling of the external bulge of the hypothenar eminence, elicited by scratching the skin on the anterior surface (ulnar side) of the forearm with a pointed instrument, is held by McCarthy to be very suggestive of pulmonary tuberculosis, and may occur only on the affected side. This author has also found Chvostek's phenomenon, rapid contractions of the fibrillæ of the facial muscles, elicited by tapping over the distribution of the facial nerve, present in 16 out of 287 cases of pulmonary tuberculosis. These phenomena depend upon the hyperirritability of the peripheral neuronic system. Tabes dorsalis, multiple sclerosis, and general paralysis have been attributed to the tuberculous intoxication, but without sufficient reason.

**Neuritis.**—The peripheral nerves are seldom affected, and sensory are much more frequent than motor disturbances. The frequency of neuritis is difficult to determine, as many are found at autopsy to have neuritic changes of degeneration, which during life cause no symptoms (latent neuritis), and occur chiefly when cachexia has developed, but whether they are due to the toxins of the tubercle bacillus, of the secondary organisms, or of the softening lung is still unsettled.

The lesion can be limited to a single nerve, a plexus, or involve all the peripheral nerves. The leg is usually more affected than the arm, and the external perineal nerve may be the first affected. Atrophy of the affected muscles occurs, but usually a few are spared in an extremity, and so some motion is preserved. Paræsthesia often precedes this type. Sensory neuritis may affect the skin, muscles, periosteum, and joints, or an entire extremity (acroparæsthesia). Neuralgia of the intercostal nerves, the trigeminus, of the sciatic and other nerves are common. Arthralgia, melalgia, myalgia, and dermalgia all occur. Tenderness on pressure over the nerves is not always present, but if continuous sensitiveness to external pressure, or to active or passive movement, especially to movement which stretches the nerves, exists, if spontaneous pain occurs, if the pain be continuous for a week

in spite of local therapy, and if the deep reflexes be lost, a neuritis is usually present. If, however, the pain be not constant, and if in the interval pressure or movement causes no pain, if it yields to relatively slight therapeutic measures it is due to an irritative cause and not to inflammatory neuritis. The mononeuritis frequently heals, but a polyneuritis is usually fatal, either quickly or, more commonly, after many months.

Pressure neuritis may occur in the vagus, due to enlarged bronchial glands, and is manifested by rapid pulse, cough, dyspnœa, hoarseness, and laryngeal spasm or paralysis. Pressure on the sympathetic by retraction or thickening of the pleura may, by its cervical and brachial connections, cause a dilatation or contraction of the pupil or neuralgia in the arm. Dilatation of the pupil may occur before the pulmonary symptoms are manifested. Pressure of glands upon the recurrent laryngeal nerve may cause hoarseness.

Pulmonary disease can cause, as Head has shown, referred pains, irritative phenomena, hyperalgesia and neuralgia, in the skin of the neck and thorax by the connections of the sympathetic and vagus. Connection with the trigeminal nerve may cause pain in the forehead, eyes, and head. The neuralgic pain may occur suddenly, dart from front to back, is little affected by ordinary breathing, but may be by deep respiration. Pressure lessens the pain, which is most frequent in the initial stages, but may recur temporarily during a relapse.

The vasomotor nerve supply is very unstable, and limited redness of the skin, especially of one cheek on the affected side or of both cheeks, elevated temperature in limited areas, localized asphyxia, sweating and ecchymosis, and a syndrome closely simulating exophthalmic goitre, are all probably the result. Myoidema is probably a functional nervous derangement of the muscles. Hoarseness, especially the premonitory type, depending upon a weakness of the adductors, is due also to the same cause.

*Sexual desire* is held by many to be increased, but this is in all probability rather due to the fact that pulmonary tuberculosis usually attacks young adults in the prime of life, and that the treatment consists of overfeeding or at least of abundant feeding, enforced rest, and lack of occupation. It is usually decreased.

*Herpes zoster*, due to changes in the posterior root ganglion, is not rare. It is most frequent in the ninth to the twelfth dorsal segments, but occurs on the face, and in one patient extended over the right leg as low as the knee. The discomfort is often slight, but the pain may be so severe that the patient has to be kept under the influence of morphine for several days. There seems to be no connection between the site of the pulmonary lesion and the affected side. In some cases the hemorrhagic variety occurs.

*Headache* is of frequent occurrence (in about 10 per cent., Cathala) and is often stubborn, hard to control, and seems to bear no relation to the extent or stage of the tuberculosis. It may be so severe that sleep is lost but this is rare.

Headache is frequently due to overuse of the eyes with poor muscle balance or weakened musculature, but is said to occur from functional disturbances as well as from organic lesions.

**Sleep.**—Insomnia is not infrequent. Change from an active to a quiet life, indigestion, cough, sweats, and more rarely pleurisy may all contribute; but neurasthenia and nervousness are most frequently the cause. It often occurs periodically, and high altitudes in some cases greatly increase it.

**Cough.—Frequency.**—Cough is the most frequent and, as a rule, the most constant of all symptoms in pulmonary tuberculosis. It usually first draws attention to the lungs, but a slight cough may exist for months and attract little notice. Its absence is more important in diagnosis than the absence of either night-sweats, emaciation, loss of strength, or dyspnœa. A cough caused by deep breathing should always be looked upon with suspicion. Aufrecht believes cough is not a symptom of the initial stage, but is rather to be looked upon as a complication, caused by laryngeal catarrh; Flick, that it is due only to breaking down of tissue or to secondary infection. In rare cases cough is absent throughout, and not very infrequently a patient is seen with a well-marked cavity whose cough has passed entirely unnoticed.

Other things being equal, the cough varies in frequency with the amount and character of the expectoration, but no direct relation exists between the gravity of the disease and the severity of the cough. It depends to a considerable extent, however, upon the part affected and the nervous excitability of the patient. Cough and expectoration may both increase during the menstrual period, and youth as well as fever seem to increase the cough. The mucosa of the respiratory tract is not equally sensitive throughout, and is most irritable in the posterior interarytenoid space at the bifurcation of the trachea. The irritability decreases downward, but an irritation once begun may rapidly increase and spread to parts showing previously slight susceptibility. The pulmonary tissue has little or no sensitiveness. It is probable that when the primary focus is situated near one of the main bronchi which becomes involved early the cough is more severe. Involvement of the bronchi is often present in cases with severe cough. In some instances the patient can select a definite point on one side as the origin of irritation causing cough. An acute pleurisy rarely causes and frequently checks cough, but a chronic pleuritic irritation may produce a dry, hacking cough.

**Varieties and Cause.**—Cough in the majority of cases is at first short, dry, hacking, not hard, and rather frequent. It may occur throughout the day or more frequently be limited to the early morning hours or night. As the disease progresses the cough becomes looser, productive, and in many cases more frequent, especially when softening is taking place. In patients with a catarrhal onset the cough is frequently loose from the onset. The character varies with the amount of secretion and the part of the respiratory tract affected. Before the bronchi are affected the cough is usually dry, short, and hacking; after they are affected the cough is similar to that in simple bronchitis. Cough may be divided into dry and moist or productive. A dry cough may be due to irritation of the respiratory tract or to a reflex.

The *productive cough* is caused by the irritation of the mucosa, usually by the slowly or rapidly collecting secretions. The morning cough is usually the result of the irritation of the sputum slowly gathered during the night. Change of position and sudden contact of the secretions with other parts of the mucosa no doubt play some part. This is true in many cases with cavity, where either a change in position or an overflowing of the cavity causes continuous cough until the vomica is emptied.

The explanation of the cough frequent with many patients *on retiring* is more difficult. Sudden contact of the secretions with parts of the respiratory mucosa hitherto for a time free, impact of air on parts of the larynx previously protected, congestion of the larynx due to the position of the head, hyperæmia of the internal organs due to contraction of the peripheral vessels

from the contact of the skin with the cold sheets, increased difficulty of expectoration, hyperæmia and consequent increased irritability of the respiratory centre (which is lessened during sleep), have all been offered as explanations. Many patients cannot sleep on the affected side, due possibly to the increased blood supply.

In a few patients cough continues to be noticed *after meals*, especially after breakfast, when it has ceased at all other times. This is due chiefly to the hot fluids taken with the meal, but increased cough may occur from food by irritation of the upper respiratory tract, rendered more sensitive from inflammation or ulceration, either by direct contact with the food or by the movements of the œsophagus or pharynx, by direct pressure upon the trachea or bronchi by enlarged glands as masses of food pass by them, by the temperature of the food, by the pressure of the distended stomach upon the diaphragm, or by the inhalation of steam from warm drinks. Increased frequency of respiration is a common cause of cough. Laughing, singing, rapid talking, fast walking, and deep breathing may all cause cough.

*Paroxysmal cough* may be due to the emptying of large cavities, to ulceration at the tracheal bifurcation, or to irritation by enlarged bronchial or mediastinal glands. The respiratory efforts are not so close together, but fully as prolonged and as exhausting as in whooping-cough.

The *emetic cough* is common in advanced stages. It is most frequent in the morning, but may occur after each meal and lead to rapid emaciation. The stomach plays a passive part and the vomiting is largely mechanical. The cough causing the vomiting may be dry.

*Nervous cough* is often continuous and irresistible, without any intervals between the paroxysms. It usually increases suddenly and often is absent at night, and can last for months with little effect upon the general health. It is dry and high-pitched, and is frequently replaced by other nervous symptoms.

The untoward results of cough are numerous and in some instances serious. Involuntary passage of the urine is not uncommon in women, but involuntary discharge of the fæces is rare unless the sphincter is weakened. Dyspnœa and cyanosis are frequent and emphysema may occur. Pneumothorax and subcutaneous emphysema are both in part the result of cough. Pain in the chest from excessive cough is common and the abdominal wall may become very tender. The excessive exercise from coughing may completely exhaust the patient and produce profuse sweats. Hæmoptysis due to increased blood pressure may be traced to cough as well as cerebral congestion and hemorrhage. Hernia, displacement of the uterus, and even abortion may be caused by it. Aspiration of a fluid sputum into healthy bronchi may take place during paroxysmal cough. Tachycardia due to severe coughing is more frequent in early than in late stages.

**Expectoration.**—Few symptoms are more troublesome than this. It is closely associated with cough, and many patients cough simply because they must expectorate. In a few cases from the outset and in many only after much training will the patient allow the sputum to collect just below or in the larynx, when by clearing the throat it can be raised. Bronchorrhœa is sometimes a distressing symptom, and the patient may be forced to spit day and night, losing much sleep and strength in consequence. The rales in the trachea due to tenacious mucus may prove very annoying, especially when the patient retires. This often persists and in fact may be accentuated

as progress is made toward recovery. In a few cases slight expectoration may be the only symptom, and it is not rare to have attention called by hæmoptysis to a small quantity of sputum in the morning which, on examination, is found to contain tubercle bacilli. As the disease becomes arrested the sputum may be the only symptom remaining, and it may persist for months or even years, and after the disappearance of tubercle bacilli. Destruction of the cords (true and false) renders expectoration much more difficult. If the amount of expectoration is out of proportion to the strength the condition is grave, and when weakness is pronounced it is impossible for the patient to raise the sputum. The relation of the extent of physical signs to the amount of sputum is very uncertain, for patients with slight signs may have profuse expectoration, and vice versa. Patients with moderately coarse "moist" rales over an entire chest may be entirely free from expectoration, due either to the fact that the rales are pleuritic in origin or to absorption of the secretions in the lungs. The latter can hardly take place when the sputum contains tubercle bacilli.

**Respiration.**—This is usually quickened and rarely falls below 20 or exceeds during rest 30 per minute, except with an acute exacerbation or in far-advanced stages. It is astonishing to see the amount of pulmonary involvement present without dyspnœa except on overexertion, although marked dyspnœa may be present without physical signs.

The majority of all patients, however, are short of breath on exertion, and a rate of 95 per minute has been recorded (Damaschino). In many early cases this symptom is noticed only on hill-climbing, rapid walking, or running. Later in the disease, emotion or exertion may produce violent dyspnœa, but orthopnœa is very rare. Patients with a nervous temperament usually have more rapid respiration, and with previous emphysema the dyspnœa is usually greater. Lebert found dyspnœa pronounced in 20 per cent. of his cases, distinct in 50 per cent., and absent in 30 per cent. Oppression in the chest may be present without dyspnœa.

The causes of shortness of breath, apart from fever and toxæmia, may be classified as follows:

1. Rapid extension of the disease (mechanical, or pressure of tubercles on the vagus): (*a*) Bronchopneumonia; (*b*) Miliary tuberculosis.
2. Changes in the circulatory system: (*a*) Anæmia; (*b*) Palpitation; (*c*) Cardiac weakness and œdema of the lungs.
3. Chronic fibrosis of the lungs or thickened pleura, followed by enlarged right heart with or without cyanosis.
4. Emphysematous pulmonary tuberculosis.
5. Complications: (i) Respiratory tract—(*a*) Pneumothorax; (*b*) Pleurisy (dry or with effusion); (*c*) Hæmoptysis; (*d*) Hyperæmia; (*e*) Bronchitis; (*f*) Aspiration of secretion; (*g*) Pressure of enlarged glands on the vagus, bronchi, or trachea. (ii) Abdomen—(*a*) Pregnancy, new-growths; (*b*) Meteorism, ascites.

The cause is most frequently mechanical, and is due to the involvement of lung tissue and the lessening of the complemental air space. An obliterative pleuritis, or a tracheobronchial adenopathy, may produce marked dyspnœa. Serous effusion, accumulating very gradually, and, in a few cases, pneumothorax, cause no respiratory distress. Aspiration of secretions into the air passages may cause pronounced dyspnœa. Dyspnœa seems to be due less to the extent than to the rapidity of the involvement, less to the stage

than to the extent of the lesion, and is most pronounced in those cases where miliary tuberculosis of the lungs supervenes upon a chronic process. Shortness of breath is influenced mechanically by food, and when it occurs later during digestion is more probably due to slight abdominal distention than to the entrance of the chyle into the blood, as Andral suggested. The lack of dyspnœa in many advanced cases is no doubt due to the fact that the lessened volume of blood needs less respiratory surface for proper oxygenation.

Dyspnœa may be toxic in origin. With a rise in temperature the rate of respiration is usually increased and the depth diminished, but in many instances this is due to an increase in the pulmonary involvement. Anæmia may be the cause in a few patients.

In chronic forms, cardiac weakness, dilatation of the right heart following a fibrosis of the apices, or thickened pleura may cause pronounced dyspnœa. Palpitation or cardiac weakness in debilitated patients is also a cause. Pain in the chest in many instances causes rapid, shallow breathing and attendant dyspnœa, as also the onset of pneumothorax.

The relation of the respiration to the temperature and pulse is not constant. The respiration rate usually increases in the afternoon or evening and may follow closely the temperature curve, but is generally independent of the actual temperature. The pulse-respiration ratio is commonly 1 to 3 or 4, but varies from 1 to 2, to 1 to 7 or 8. The extremes are often in persons of unusual stature (Fox). As the pulse usually follows the temperature rather closely, ratios of 1 to 2 occur more often with low temperature. Marked change in the ratio in either direction is unfavorable. Cheyne-Stokes breathing is rarely met with except when meningitis has occurred. Biot's type of breathing occurs shortly before death.

**Hæmoptysis.**—While often applied to a spitting of blood from any source, hæmoptysis is here used to denote a spitting of blood which has escaped into the air passages below the larynx.

Its relation to pulmonary tuberculosis has long caused much discussion, and not until the discovery of the tubercle bacillus was it finally settled that hæmoptysis did not cause pulmonary tuberculosis. Hippocrates, Galen, Aretaeus, Boerhaave, and Van Swieten thought pulmonary tuberculosis followed hæmoptysis, while Richard Morton in 1689 doubted it, and Portal, Bayle, Laennec, and Louis denied it. Andral occupied middle ground, and Graves, followed by Hoffmann, Niemeyer, and Reginald Thompson, revived the first view, which was that the blood itself could produce caseous nodules, and Weber, Baumler, Carswell, and Rokitansky upheld them. Traube and Walshe, however, early held to the view that pulmonary tuberculosis always preceded the hæmoptysis, as signs of previous failing health were found in the majority of the patients. Traube also called attention to the fact that if blood caused pulmonary tuberculosis the signs should be most frequent at the base and not as they are at the apex. Weber and Reginald Thompson advanced elaborate theories, explaining the possibility of the blood reaching the apex through aspiration. On the discovery of the tubercle bacillus, Williams found this organism in the blood, and later researches have shown it to be present in a proportion of all cases, settling the cause of the rapid extension of the disease that follows some hæmoptyses.

**Frequency.**—This may be said to be about 60 per cent. of all cases, but varies according to different authorities from 24 per cent. to 80 per cent. In 2344 patients at the Phipps Institute it occurred in 48 per cent. Age has

a marked effect upon the frequency. It is rare before puberty, but a fatal case has been reported in an infant of ten months (Hoffnung). In old age hæmoptysis is also uncommon, but probably more frequent than in infancy and childhood. Sex and age together seem to exert some influence on its frequency. In 905 males at the Adirondack Cottage Sanitarium, 49 per cent. had hæmoptysis at some time. Of those under twenty years of age, 43 per cent. had it; of those from twenty to twenty-nine years (495), 54 per cent.; from thirty to thirty-nine years, 45 per cent., and over forty years, 38 per cent. Hérard, Cornil, and Hanot state that hæmoptysis is as common after forty years as before. Among 890 women, 40 per cent. suffered from hæmoptysis, as follows: according to age, under twenty years, 47 per cent.; twenty to twenty-nine years (502 cases), 39 per cent.; thirty to thirty-nine years, 38 per cent.; over forty years, 48 per cent. Of these 1795 cases, 45 per cent. had hæmoptysis. A comparison of the figures shows that while in males more hæmoptyses occur in the third decade, in females more occur before twenty and after forty. It also shows that more males than females have hæmoptysis, and that in males this symptom occurs more frequently in the years of greatest activity.

It is said to be more frequent in tall individuals than in short. This was no doubt suggested by the fact that many patients who have a "phthisical build" are above the average height. Of 174 males at the Adirondack Cottage Sanitarium under 5 ft. 8 in. and of 183 males over 5 ft. 8 in., 50 per cent. in each instance had hæmoptysis. The same was practically true for the females, 34 per cent. of those (148) under 5 ft. 4 in. and 39 per cent. of those (168) over 5 ft. 4 in. had hæmoptysis. There seems, therefore, to be no connection between height and hæmoptysis.

Hæmoptysis is an accident which may occur in any form of pulmonary tuberculosis, and is not a sufficient basis for classification. In the more acute varieties it is much less common, but occasionally ushers in an acute process engrafted upon a chronic form. Fowler has reported a fatal case occurring in acute miliary tuberculosis, and A. Fränkel one in pneumonic phthisis. It is said to occur most frequently in the early stages of the chronic pulmonary form, and severe hæmoptysis is said to be most frequent in the first three months of illness (Pollock), but this may be questioned. Patients with a family history of tuberculosis seem very little more liable than those without this taint. It is unusual to find a patient who has had but one hæmoptysis, and some patients, usually those semi-arrested, have a marked tendency to it. Many of them do well, and Andral reported a case where hæmoptysis occurred from the twentieth to the eightieth year. At autopsy numerous calcified tubercles were found in the lungs.

The connection between hæmoptysis and physical signs is notoriously uncertain. It may be severe in patients without physical signs, and a fatal case has been reported in a child where the total area involved could be covered by the tip of the finger (Fowler). On the other hand, patients may have extensive ulceration and large cavities in both lungs without hæmoptysis. In sanatoriums and open health resorts it has frequently been noticed that it is usual for several patients to have hæmoptysis about the same time; in other words, an epidemic of hæmoptysis.

**Site and Pathology.**—The distinction between bronchial and pulmonary hæmoptysis, so long insisted upon by some writers, is of little value. Small hæmoptyses, bloody streaks in the sputum, can unquestionably come from

the bronchi, but more blood than this comes almost invariably from the pulmonary vessels. Pink and rusty sputum may be due in many cases to diapedesis from the bronchial or pulmonary capillaries, and, while usually not serious, may prove fatal (Fowler). Such sputum, however, is most common after hæmoptysis of larger amounts. Some (Rindfleisch, Ruehle and Sée, Aufrecht) hold that the lumen of the pulmonary vein (more rarely the artery) in some early cases is narrowed by a tubercle in its walls, and that there is a consequent rise of blood pressure, especially at this point, where the rupture occurs. Fatal hæmoptysis from ulceration of a vessel wall without the formation of an aneurism is exceedingly rare, and some of the reported cases are probably due to the fact that the aneurism has been completely detached from the vessel. Trained observers rarely fail to find a ruptured aneurism in fatal hæmoptysis (in 70 out of 80 cases, Kidd).

These aneurisms are nearly always found on a middle-sized branch of the pulmonary artery, rarely on the pulmonary vein, and then early in the disease, and more rarely on the bronchial artery. The larger vessels, owing to more elastic tissue, resist erosion, at least until thrombosed. The aneurisms are globular, rarely fusiform, and occur generally upon the unsupported side of a vessel in the wall of a small cavity, which they may fill. For this reason some look upon severe hæmoptysis as a sign of cavity. Their size, usually that of a large pea or small cherry, seldom exceeds that of a small walnut, and, while frequently single, they may occur in numbers (22 in one case, Kidd). Aneurisms may be found in the walls of the bronchus. They are most frequent in the middle area of the lung, near the periphery, *i. e.*, the lower part of the upper lobe (more common) or the upper part of the lower lobe, where the pulmonary movement in respiration is greatest (West). The rupture usually occurs at the distal boundary of the dilatation.

**Amount of Blood.**—The amount of blood varies from the slightest trace to several liters (in one case 9 liters were lost in 50 days; in another, 3 liters at one time). It is usually slight in amount, and in 2882 (69 per cent.) of 4125 cases of hæmoptysis at Brompton Hospital the amount was less than ½ ounce (15 cc.). The blood, usually frothy, may be coughed up by mouthfuls every few minutes for days, or it may come up in a gush and pour out of the mouth and nose and large quantities enter the stomach. In some cases the blood slowly collects in a cavity, finally overflows, irritates the mucous membrane, and is then coughed up. In rare instances with large excavation, the patient may die from hemorrhage into the cavity, with little or no hæmoptysis. Usually, however, a few ounces of blood are expectorated, frequently at night, and the patient may be awakened. Hæmoptyses seldom occur singly, and generally two to four follow each other in the course of five or six days. The sputum is almost invariably blood-stained for several days afterward.

For clinical purposes it is sufficient to classify hæmoptysis as streaky, slight (more than streaks and less than 30 cc.), moderate (30 to 100 cc.), severe or copious (100 to 250 cc.), and profuse (over 250 cc.). These amounts refer to the quantity of blood lost in twenty-four hours. In 50 per cent. of all cases the hæmoptysis is streaky, in 15 per cent. moderate, and in 10 per cent. severe and profuse. As 25 per cent. of all patients have no hæmoptysis, it is an urgent symptom in about 10 per cent. (West). It is not possible to estimate the size of the bleeding vessel from the amount of blood lost.

The blood varies in color from bright red to very dark, depending more upon the time it has remained in the lung than upon its origin. In any case bright-red blood cannot be said positively to come from a vein, as the bronchial arteries contain such blood. The blood is rarely clotted at first, although in some instances no fresh blood is ever raised. As the hæmoptysis ceases clots are more frequent, and in some cases casts of the bronchi which may cause dyspnœa are expectorated. The expectorated blood usually clots quickly and is alkaline. Ortal has found that the blood in some cases possesses the power to agglutinate tubercle bacilli. The bacillary contents of the blood vary considerably, but, as Williams first showed, it often contains tubercle bacilli, and in a "primary" hæmoptysis should always be carefully examined. Recent work by Flick, Ravenel, and Irwin has shown that pneumococci and streptococci are frequent in the blood.

The *causes* may be divided into intrinsic and extrinsic. The former, the underlying factors in every case, have to do with the pathological changes in the vessel wall. Hæmoptysis other than capillary never occurs unless the vessel walls are weakened by disease. In some cases the vessels seem to be hereditarily weak, and these patients may suffer from frequent hæmoptysis. Extension of the disease process into the vessel wall usually occurs in the lung, but diseased glands may ulcerate into a vessel and expulsion of lung stones seems in some instances to be connected with hæmoptysis.

The systemic blood pressure is much lowered in most cases of advanced pulmonary tuberculosis, but the pressure in the pulmonic system is in many advanced cases apparently raised and an accentuation of the second pulmonic sound is frequent. The frequency of the pulse is often in inverted relation to the arterial pressure. In advanced stages the diminished volume of blood reduces the frequency of hæmoptysis. Naumann investigated 100 cases of pulmonary tuberculosis, 69 of which had high blood pressure (measured by Gaertner's tonometer). Of these, 44 (or 63 per cent.) had hæmoptysis. Dividing these cases into stages (Turban), 85 per cent. of the first, 55 per cent. of the second, and 42 per cent. of the third stage had hæmoptysis, showing that it is most frequent in early cases with high blood pressure.

In the majority some rapid increase of blood pressure is held necessary for its production. This is generally thought to be afforded by some extrinsic cause, such as violent exertion, particularly of the arms and thorax, or violent respiratory and general exertion, such as is entailed in mountain climbing. It is a singular thing, however, how rarely hæmoptysis follows immediately on any single act of overexertion, and a large percentage (nearly 80 per cent.) cannot be connected with overexertion. Two-thirds are said to occur during quietude, and the rest, with but rare exceptions, only during that degree of physical effort or mental excitement usual in ordinary life (Powell). Colin has shown that on exertion the pressure in the pulmonary artery is increased much more rapidly than in the aorta. Hæmoptysis can be divided into two classes: in one it seems to be an accident in the course of the disease, and in the other it is simply one of the symptoms of an acute exacerbation. When it is accidental the same fact holds true, that a large majority seem to have as yet no definite cause and are certainly not connected with exertion.

Hæmoptysis occurs frequently in the early morning hours, a time when the blood pressure in the pulmonary system is subject to marked variations. Some, however, can be traced to prolonged overexertion, but occur

many hours later (twenty-four to seventy-two). Emotion stands in a somewhat similar relation.

An attempt has been made to connect hæmoptysis with barometric changes —wind, moisture, precipitation, sunshine, and cloudiness—and combinations and quick variations of them; but this has so far failed. High elevations are said to have no effect upon its occurrence, but patients who exercise immoderately on arrival are more liable to it than in lower elevations. Suppression of blood, either from hemorrhoids or from menstruation, has been held as a cause. However it may be, hæmoptysis frequently occurs in women about the menstrual period, and some patients have slight hæmoptyses every month over long periods. These often have little effect upon the general health, and cease usually when the disease is fully arrested. Coitus may cause hæmoptysis (Plique). Irritant gases may be a cause, and one case was observed where small hæmoptyses occurred twice after the administration of ether. Exposure to the sun has been said to cause it. Much stress has been laid upon the seasonal variation of hæmoptysis, and many efforts have been made to connect the occurrence with winter, summer, or spring and fall. It is more frequent (Gabrilowitsch) during the spring and fall, and the sudden thermometric and barometric changes have been adduced as the causative factor.

Recently, Flick, Ravenel, and Irwin have drawn attention to the frequency of the pneumococcus in the blood of hæmoptysis and in the sputum of many patients who suffer from it. In pneumonia rusty sputum is common, but brisk hæmoptysis rare. The seasonal incidence of pneumonia closely follows that claimed by some for hæmoptysis, and this work is suggestive. The examination of all sputum for the pneumococcus and the isolation of patients with hæmoptysis and of those in whose sputum the pneumococcus is abundant would follow naturally if this work be confirmed.

The immediate *effect* of hæmoptysis depends upon the quantity of blood lost, the amount of fundamental disease, and the complications. The effect on the ultimate termination is very variable, and no matter how severe or how slight hæmoptysis has been, it is well to give a guarded prognosis. A slight hæmoptysis may be the precursor of a severe and fatal bleeding from the lungs, but as a rule the earlier the stage the less serious the prognosis, which after twenty-four to forty-eight hours is more favorable, as by this time a thrombus can form. In a few cases hæmoptysis is followed by some improvement—fall of temperature and loss of feeling of oppression; often this is only temporary. Heart action which produces high blood pressure and consequent hæmoptysis is also favorable to healing. An initial hæmoptysis is often of advantage to a headstrong patient who, thoroughly frightened, is willing at once to take all precautions. For this reason it is wise not to pass over an initial hæmoptysis lightly. It is difficult to see how hæmoptysis can cause an "elimination en masse of the tubercle bacilli, and thus finally effect a cure," as some (Knopf) have affirmed.

In a much larger proportion, hæmoptysis seems to exert no effect whatsoever upon the immediate course and appears to be simply an accident. Except a few days' rest in bed it entails no discomfort upon the patient.

In some it has to be considered as simply one of the symptoms of a progressive lesion, with accompanying dyspnœa, rapid pulse, and elevated temperature. In this case the most usual occurrence is an attack of tuberculous bronchopneumonia of more or less severity. Aspiration of the blood

into a whole lobe is rare and affects the lower lobes more frequently. The resulting pneumonia may be due to the secondary organisms, and run a more or less atypical course, or to the tubercle bacilli, when the result is much more serious. The fear and consequent behavior (great agitation and refusal to follow advice) of some patients seem to have a marked influence upon the frequency of this complication, although the amount of blood is also of importance. The entrance of pus and secondary organisms into the circulation can take place through the rupture.

It is not unusual after hæmoptysis to have great dyspnœa, rapid pulse, high temperature, cyanosis, and death in a few weeks from acute miliary tuberculosis of the lungs. In fact, any bleeding followed by one of these four symptoms is to be looked upon as serious, and an absence of these indicates that little immediate fear need be entertained. Slight fever usually occurs for a day or two, due no doubt to the absorption of exuded blood. Profound prostration may follow the loss of a slight amount of blood when no physical signs are to be detected. A profuse hæmoptysis may turn the tide against the patient.

Death may result from loss of blood, either immediately or in a few days or weeks, and comprises about 2 per cent. of all deaths in pulmonary tuberculosis. According to Williams, fatal hæmoptysis is nearly twice as frequent when softening begins and nearly five times as common where there is excavation. It is much more frequent in males and with rare exceptions comes from a ruptured aneurism. When bleeding takes place from a vessel on the side of a large cavity it may be fatal and hæmoptysis slight or absent. In other cases the blood pours out so rapidly that death from suffocation follows, the common cause in fatal hæmoptysis. Cerebral anæmia and syncope is a more common cause of death than exhaustion. Death from shock or acute anæmia is of rare occurrence.

So much has been written upon hæmoptysis as a favorable symptom that it has been deemed wise to abstract the conclusions of an analysis of 1810 cases from the records of the Adirondack Cottage Sanitarium. This shows that males with hæmoptysis did not do as well during sanatorium residence as those who had no hæmoptysis. In the females no difference could be noticed. A study of 1276 cases discharged from the institution two to twenty years previously shows that for males a slightly larger number of deaths have occurred among those who had hæmoptysis, while for the females this is not so. Von Ruck found unfavorable results in 70 per cent. of all cases with hæmoptysis. Hemorrhage from the lung can take place into the pleura, and some (Sticker, Dieulafoy, etc.) hold that spontaneous hæmatoma of the pleura is almost always the result of a preëxisting pulmonary tuberculosis.

**Pain.**—Few patients whose disease runs a more or less chronic course escape thoracic pain. Hérard and Aufrecht found it in two-thirds of their cases. In 1513 patients at the Phipps Institute, Philadelphia, 71 per cent. had some pain, including that referred to the extremities. It may be the first or throughout the most pronounced symptom and should always receive careful attention.

The cause is very uncertain, and is said to be due to pleurisy, neuralgia, neuritis, myositis, nervous erethism, pulmonary congestion, pressure from enlarged glands, localized fatigue of the muscles used in respiration or in coughing, extension of inflammation to the intercostal nerves, contraction of

old cavities, traction on pleural adhesions or on the heart, pneumothorax, tuberculosis of the rib, as well as to the intrapulmonary disease (the referred pain of Head).

Pain over the upper front is most frequently referred or due to acute pleurisy or to traction on pleural adhesions. Pain over the base of the lung is usually pleuritic, while pain in the interscapular area may be referred, due to pleurisy or to pressure from enlarged glands. Pleurisy is not always accompanied by pain, as the friction can at times be heard several feet from the patient and cause little or no discomfort, but pulmonary tuberculosis is practically always accompanied by pleurisy, and it is an exceedingly rare thing to find no pleural adhesions at autopsy. Pleuritic pain may be severe or slight, may occur only after a deep inspiration, expiration, cough, sneeze, or yawn, or may be continuous and every breath be attended with pain. This pain varies from a vague discomfort, a sense of pressure or of tension, to a sharp, lancinating pain which cuts the breath short and produces sweats and great prostration. It may occur in any part of the chest, but is most frequent in the interscapular, subclavicular, and infra-axillary regions. The pain may be noticed upon the opposite side, in the epigastrium, the hypochondrium, the sacrum, the shoulder on the affected side, and even radiate down the arm (diaphragmatic pleurisy). Singultus is not frequent. Slight pleuritic pain is often accompanied by a short, hacking cough and fever. A sudden cessation of pain suggests fluid.

The pseudopleural rub of Rosenbach, heard over the complementary space, existing between the lower border of the lung, the diaphragm, and the chest wall in patients with wide intercostal spaces, is believed by many to be due to muscular contractions, and Fränkel holds that Koll's sinus-pleuritic is the same phenomenon. Hodenpyl, however, found nodules and patches in the pleura which he believed were the results of tuberculosis in nearly 50 per cent. of 91 adults who had no pulmonary tuberculosis.

Patients often complain of pain that cannot definitely be said to be due to pleurisy, and in many cases is no doubt the referred pain of Head. The site varies, but it usually occurs on the affected side. The most common locations are the infraclavicular area to the third rib, the interscapular and the infra-axillary regions. Pain also occurs, but less frequently, at the apex, in the suprascapular and subscapular areas, and may radiate down the arm. Cases have occurred where angina pectoris was suspected from the localization of the pain. The character of the pain is very variable, being most frequently a slight feeling of discomfort, of localized fatigue, or soreness. It may be constant in location and time and last for days, months, or even years. It is most frequently fleeting, difficult in some cases to localize, and in others so variable in its location that the pain is thought to be "rheumatic." The pain in some instances escapes the patient's notice until a physical examination is made and percussion begun. In other instances deep pressure is necessary to elicit it, and again the skin may be so sensitive that the slightest touch causes severe pain, the clothes cause great discomfort, and the patient lies on the opposite side. In these cases of hyperæsthesia the skin is often very sensitive to pressure between the fingers. At times the pain is described as going "through and through." In many cases the pain is independent of the respiratory movement, in others it is increased on any unusual respiratory movement, and is frequently noticed only on coughing, yawning, or sneezing.

Pain often precedes hæmoptysis and may disappear on its occurrence. Intercostal neuritis with the classical points of tenderness is rare. An intercostal myositis has been described by Coplin and by Aufrecht. Louis attributed the pain in some instances to tubercles in the lungs, and Andral the pains which appeared with fever to the softening of tubercles, but the only pains connected with the pulmonary parenchyma are the referred pains of Head. Sokolowski, however, when stubborn pain, with poor general condition, chills and fever are present, believes a deep focus is extending toward the periphery of the lung. Severe pain from herpes zoster (before the eruption of the rash) or from pneumothorax (when many adhesions are present) may not be attributed to the proper cause for some days. Pain due to cough about the thorax, over the insertion of the diaphragm as well as in the abdominal and dorsal muscles, is not uncommon.

**Voice.**—Changes of the voice are of frequent occurrence. The slight "prodromal" hoarseness, often only temporary and fleeting, but recurring, may be the first indication of the pulmonary disease. The larynx may be perfectly normal, as 1 out of every 12 patients with pulmonary tuberculosis suffering from hoarseness shows no laryngeal changes (Gerhardt). In advanced stages the voice often becomes weak, is easily fatigued, and on prolonged use may disappear. The quality is often changed and some thickness or hoarseness is common. In other cases the voice is strong until death. Excluding tuberculous laryngeal changes the cause of the hoarseness has been attributed to nervous conditions (one-third of cases, MacKenzie), neuritis of the laryngeal nerves, atrophy of this nerve (more commonly of the right, due to pressure upon it from pleural thickening, apical contraction, enlarged glands), laryngeal catarrh, or straining of the cords through severe cough, and collection of irritating sputum upon the cords.

## THE PHYSICAL SIGNS OF TUBERCULOSIS.

The chief importance of these relates to diagnosis. Physical signs of little or no significance alone when coupled with certain symptoms are of the greatest value, and every general practitioner should be constantly on his guard against error, as carelessness and the use of faulty methods of examination are the chief reasons why the early physical signs are overlooked. To a limited extent the physical signs vary with the time of day, especially in some advanced cases. It must be emphasized that in most early cases at least comparison of the two sides is of more importance than comparison with a more or less hazy standard. At the outset it should never be forgotten that extensive lesions, situated centrally, may produce only very slight or even no physical signs. Repeated examinations may be necessary to discover all the physical signs present at an early stage. The time of day of the examination should be always noted and future examinations made when possible at the same hour. The morning is to be preferred, as rales may be more frequent, and daylight is always to be preferred.

**Inspection.**—The patient, stripped to the waist, and covered with a chest cloth or blanket, should be placed in a warm room, either sitting (preferably on a revolving stool) or standing, so that a strong light fails diagonally across the chest, which should be viewed anteriorly, posteriorly, laterally, and from above.

**Shape.**—The general conformity of the chest varies from the normal to the most pronounced paralytic or phthinoid type. The shape seems to bear some relation to the stage of the disease and is a trifle long at first, with a slight prominence of the clavicle on the affected side. As the disease advances the chest becomes slightly smaller, due probably not only to emaciation, but also to change in bulk of the lungs. In unilateral disease the change in bulk of one lung may be compensated for by enlargement of the sound lung without any external manifestations.

The flattening of the chest so often seen in the late stages is in most cases more apparent than real, as can be easily observed by having the patient stand or sit erect and hold back his shoulders. In some instances this demonstrates a chest rounder and deeper than normal. The round chest with the falling forward of the shoulders often causes tilting of the scapulæ, the so-called "winged" scapulæ. In other cases flattening of the chest occurs either from above downward or from side to side, and both may be present in the same chest. The costal cartilages may be raised and the sternum depressed, forming in accentuated cases the "funnel" chest. The paralytic or phthinoid thorax is more often a result than a precursor of pulmonary tuberculosis, and may occur in other diseases. Changes due to intrapulmonary disease are most likely to be seen at the apex, those due to pleuritic disease at the base (except in children). The "pigeon" breast, funnel chest, the "barrel" chest, and the remains of infantile rickets are seen in a certain number. Emphysematous "cushions" above the clavicles are not rare. Œdema of the lower thorax is very infrequent in uncomplicated cases.

*Asymmetry* of the chest, absent only at first, is later often very marked. The vertebromammary diameter (from the nipple to the spine in the nipple plane), normally longer on the right, is reduced often on one side by the disease process. Asymmetry is best observed by comparing the clavicles. Shrinking below the clavicle is in part at least due to atrophy of the pectoral muscles. In pronounced cases the shoulder on the affected side is lower. Atrophy of the scapular muscles occurred in 32 per cent. of 776 patients (Flick). The pathogenesis of this atrophy is without doubt, Boix believes, analogous to that of arthropathic amyotrophy. Bulging or undue prominence of the affected side rarely occurs. Plate-like depressions or dimples in the inner first, second, and third intercostal spaces, due to old fibrous infiltrations or cavities, are not uncommon and the inspiratory movement of the anterior border of the right lung, when it has undergone compensatory enlargement, may be seen by a bulging of the left intercostal spaces for one-half to one inch from the sternum, while the rest of the side remains almost or quite motionless (Turban). Tilting of the clavicle on the affected side has been described in early cases.

The angle of Louis, usually present in the incipient, is often reduced in an advanced stage. The pyriform exostoses of the second costal cartilages undoubtedly mislead some into the belief that this angle is increased when it is really reduced. The angle is stated to be normally about 166 degrees, and in pulmonary tuberculosis from 172 degrees to 180 degrees. The intercostal angle, normally 90 degrees, varies from 30 degrees to 120 degrees. As a rule, the angle decreases as the disease progresses.

The intercostal spaces, normal at first, later become more marked and wider (especially on the affected side). Bulging of the interspaces occurs only when some complications arise.

The area of visible cardiac impulse increases as the lung contracts and in some instances the point of maximum impulse may be found in the left anterior axillary line, in the right midclavicular line, or even under the angle of the left scapula (Kidd). Such a picture should always suggest cavity, although pleurisy may produce marked changes. A large area of cardiac impulse in the second, third, and fourth interspaces on the left usually indicates disease of the left apex. The cardiac impulse in contraction of the left side may be invisible at times and felt only during inspiration, according to Turban, who holds that displacement of the absolute cardiac dulness three-fourths or one inch to the right (to the middle of the sternum) is a typical and cardinal symptom of right apical disease of some standing.

Slight scoliosis is often present early, with the concavity more often toward the affected side. In chronic fibroid cases the scoliosis may be marked.

**Movement.**—This varies greatly and a large excursion is often present in the early stages. Limitation of movement occurs early, and a unilateral limitation or lagging may be one of the few signs present. The movement of the chest is best noted by combining palpation with inspection. In a majority of cases lessened movement occurs first in the subclavicular fossa, and can be readily seen from in front. In other instances the limited excursion can be observed more readily by standing behind the patient seated on a stool and placing the hands over the subclavicular fossæ. A compensatory increase of movement of the lower chest on the affected side seems to occur in some patients and in doubtful cases may aid in localizing the disease focus. As the disease advances the limitation of movement is more marked, and in some cases, probably through the calcification of the cartilage, the chest moves only as a whole. Litten's phenomenon may give valuable information in regard to the excursion of the diaphragm. Staining the chest yellow seems to aid in its observation. Local retraction of the chest may occur during inspiration, due probably to pleuritic changes.

It might be added that limitation of movement is due (1) to obstruction of the bronchi and deficient entry of air; (2) to change in elasticity of the lung through consolidation or fibrosis; (3) to pleuritic adhesions or pain; (4) to calcification of the costal cartilages; (5) to weakness.

*Venous varices* are of frequent occurrence near the costal margin, where, however, they rarely form an "emphysematous girdle," and more occasionally are found over the upper chest, front and back. They are said to occur more frequently upon the affected side, although this may still be questioned. The subcutaneous veins over the upper chest may be dilated, often on one side, probably due to constriction of the intercostal veins through pleuritic inflammation and return of the blood through the anastomotic channels to the superficial vessels. Excessive sweating in the axillæ is frequent.

A *difference in the size of the pupils* occurs at times (in 15 of 181 incipient cases), and the larger pupil is usually on the same side as the discoverable lesion. This is no doubt due to the pressure on or involvement of the cervical sympathetic system on the affected side. Some have found the pupils more widely dilated than normal. The involvement of the recurrent laryngeal nerve may cause more or less difference in the movement of the vocal cords.

As the disease advances and emaciation becomes marked, the neck

appears long and thin, and viewed from behind gives a characteristic picture with the protruding ears. The eyes sink deep in their sockets, the sclera become pearly white, the cheek bones prominent, and the cheeks flushed (often more on one side) or pallid. The hair becomes thin and dry and the lips often cyanotic. The muscles are flabby, the skin dry and harsh, or after slight exertion bathed in a clammy sweat. The chest looks long, narrow, and flat, although often this is more apparent than real; the scapulæ are "winged," the interspaces wide and sunken, and the ribs more slanting, making the intercostal angle narrow. The fingers are often clubbed, and the patient, though still young, may appear an old man.

**Mensuration.**—This is closely connected with inspection, and much of inspection comes properly under this head. The angle of Louis and the intercostal angle should be measured by a goniometer; unilateral shrinking of the chest can be confirmed by calipers.

The *circumference of the chest* is best measured in the plane of the junction of the fifth costal cartilage and the sternum. It should be taken during quiet respiration, at the postexpiratory pause, and after a deep inspiration and full expiration. Some confusion seems to exist in regard to the terms "chest expansion" and "respiratory movement." The former should be used to indicate the difference between quiet respiration and full inspiration, and the latter that between full inspiration and full expiration. The normal expansion in health is about 1¾ inches for males, 1½ for females, the normal respiratory movement more than double these figures. Patients who have taken respiratory exercises, or who walk up graded paths, have larger measurements than those at rest, but both are in most cases below normal.

The *length of the chest* has been much discussed and in many far advanced cases, especially those with a phthinoid or paralytic thorax, is considerably increased. For the sake of uniformity it is well to measure it in the mid-clavic lar line parallel to the midline from the clavicle to the edge of the costalmargin. In healthy males this measurement is about 13 inches, in females about 1 inch less.

**Chest Index.**—Attention has recently been called by W. Hutchinson to the "chest index," *i. e.*, the relation of the anteroposterior to the transverse diameter at the level of the junction of the fourth or fifth costal cartilage with the sternum. In health this may be stated to be 73, in early stages of the disease about 72, and in later stages about 76. The index in the female is slightly lower than in the male. It can be readily changed within certain limits in the individual, increases probably as the disease advances, and has no prognostic and little, if any, diagnostic value. There is some tendency for the chest to divide into two types, one flat (index 68 to 70) and one deep and round (index 78 to 80), but both slightly reduced in size and longer than normal. The normal width of the chest at the level of the fourth costal cartilage is about 11 inches for males and 9½ inches for females, the normal depth about 8 inches for males and 6¾ for females.

Freund long ago called attention to the early calcification of the first costal cartilage and more recently Gessner has attempted to measure the superior aperture of the thorax, applying here the laws governing the relation of the external to the internal pelvic dimensions. He finds "relatively often" a stenosis, more marked in the more acute types.

The lead-tape *cyrtometer* used in conjunction with accurate calipers will give a reliable outline of the chest, which recorded on paper can be used for

comparison with future tracings. Many patients undergoing treatment show marked increase in size of the thorax. The pantograph, which produces an exact tracing of the shape of the chest in any size desired, is theoretically valuable, but practically of little use.

*Spirometry*, first introduced by Hutchinson, has not proved of much value in diagnosis, as many early cases show little change in the tidal air, but used over an extended period may aid in the prognosis of an individual case. Weight, height, and age are among the modifying factors. Von Ziemssen found the minimum in health to be 20 cc. in males and 17 cc. in females to 1 cm. in height. In more or less advanced pulmonary tuberculosis it may be decreased 12 to 60 per cent. Hall has recently devised a method by which from various measurements the vital capacity can be closely approximated. A sudden and marked reduction may indicate a new focus.

*Pneumatometry.*—Waldenburg's study of the inspiratory and expiratory forces seems to show that the inspiratory power is diminished even in incipient pulmonary tuberculosis, while the expiratory (except in extreme cases) remains normal. The reverse is true of asthma, emphysema, and bronchitis, but the diagnostic value is slight. Stanton, who has recently made a post-mortem study of the intrapleural tension in pulmonary tuberculosis, has found it to vary directly with the pleural adhesions. Sticker's thoracodynometer measures the reserve power which the respiratory muscles can exercise aside from the motions of respiration.

**Palpation.**—This combined with inspection affords the best means of determining unilaterally restricted movement. To palpate the apex it is best to stand behind the patient, and placing the thumb in the supraspinous and the fingers in the supraclavicular fossa, grasp the apex, so to speak, in the hand. The vocal fremitus is in many early cases little if at all changed from normal. If it is equal on the two sides it is increased on the left or decreased on the right, usually the former. In 94 incipient cases with a lesion on one side palpation was normal in 64, greater on the affected side in 23, and on the unaffected in 7 (6 on the left side). In more advanced cases great discrepancy seems to exist at times between signs discoverable by palpation and signs obtained by other procedures. Vocal fremitus, for instance, may be either increased or absent over a cavity. Pleuritic friction and sonorous rhonchi are rarely palpable. Markedly increased vocal fremitus usually indicates consolidation. Tussive fremitus may be of value in aphonia. Tenderness may be complained of on palpation, but is usually elicited on percussion.

**Percussion.—Methods.**—To obtain the most accurate results great care must be paid to the various procedures. With the chest bare, the patient should stand or sit in a corner or near a wall, with his arms hanging loosely by his sides and his head straight. It is best to begin with immediate percussion of the clavicles. The remainder of the two sides is then compared, and often when percussing one side it is well to go from the resonant parts below to the suspected apex. In some cases the supraclavicular fossæ can be percussed more accurately from behind. If in doubt the part should always be percussed after a full inspiration, first from one side, then from the other. To percuss the axillary region properly the patient should either clasp his hands above his head or place them on the back of his neck and raise his elbows as far as possible. Percussion in women with lax or large mammæ should be done in the prone position.

Direct percussion in many instances is helpful, especially when comparing the note of the bases behind or the clavicles. Auscultatory percussion is of little value in pulmonary tuberculosis except possibly in defining the limits of the lobes. Light percussion is best for superficial lesions; strong for lesions 5 cm. or more below the surface of the lung, which, however, even if extensive, may escape detection.

When the involvement of pulmonary tissue necessary to produce any change in the percussion note is considered the absence of dulness in the incipient stage is not strange. Cornet has stated that in general to produce any change in the percussion the area of disease should have reached an extent of 4 to 6 cm. and a depth of 2 cm. To produce flatness the focus must be at least 5 cm. in depth. Alison held that the air capacity of the lung must be reduced one-third to produce any change in the percussion note and one-half to produce dulness. Oestreich believes a single focus to produce change on percussion must be the size of a cherry. If the foci are multiple they need not be larger than a pea. All this would explain why a small lesion can be detected by percussion more easily at the apex than elsewhere.

In some cases the first change in the percussion note is a shortening of the duration, although in many cases it is already accompanied by a rise in the pitch and a diminution of the loudness. Occasionally, emphysematous changes occur which mask the dulness; even in some quite advanced cases little or no dulness can be obtained. This change is no doubt the cause of the slight relative dulness at times detected on the apparently unaffected side.

In many cases on careful percussion a slight change in note is detected at the level of the second rib. If we percuss from below upward, at this level, the note becomes slightly higher in pitch and possibly a little shorter. This is not pathological, but is due to the increased thickness of the pectorals in these areas. Slight dulness may be found in the interscapular region (enlarged glands ?) in some patients without any other abnormal physical signs ever occurring. Scoliosis, or irregular configuration of the shoulder, may cause slight dulness and apparent shrinking. Percussion over the vertebræ is not of much aid in apical dulness.

In 28 out of 201 incipient cases percussion was negative, while auscultation revealed some abnormal signs. In 107 cases with a lesion on one side, 25 cases were normal on percussion; 5 exhibited slight dulness on the opposite side; and in 1 case the note at both apices was hyperresonant. In the remaining 76 cases the change in the percussion note occurred at the apex in 73, 37 in front, 12 behind, and 24 both in front and behind. In 12 cases the change occurred only above the clavicle. In 16 cases there were slight differences on percussion without any accompanying auscultatory signs. In 3 cases there were no abnormal physical signs on auscultation. In the remaining 13, auscultation revealed some change on the opposite side.

The dulness observed in incipient pulmonary tuberculosis is usually very slight, often requires much experience to detect it, and frequently increases as the patient recovers. In more advanced cases, and especially in those whose onset was with pleuritic effusion, the dulness may be very marked and pass even into flatness. Advanced tuberculosis may exist, however, with little or no change of note. Tympany or hyperresonance may occur when small foci compress the intervening tissue, when emphysematous changes have taken place, or with cavity or complications (pneumothorax). The cracked-pot sound may be heard more frequently on the left side, over cavities

with an elastic wall situated superficially in the upper anterior part of the upper lobes. It is nearly always, when pathological, associated with some degree of dulness, and is rarely obtained elsewhere than in the region between the clavicle and the fourth rib. A quasi cracked-pot note may occur over perfectly normal regions in chests with elastic walls and normal resonance.

Increased resistance is associated with different degrees of dulness in many cases. Percussion in some instances elicits more or less tenderness, usually more marked on the side more affected. It is always advisable to determine by percussion the lower level of the lungs, as small areas of dulness in this region are readily overlooked. Lessened excursion of the diaphragm, which frequently occurs on the affected side, can be determined fairly accurately by percussion of the bases of the lungs at the end of full inspiration and expiration. The patient should be told fully what is being done to gain his assistance. It should not be forgotten that the respiratory movement increases after several full respirations. In a series of 41 cases studied to show the relative value of radioscopy and percussion in determining the diaphragmatic movement the two methods proved to be of nearly equal value. Litten's sign is much less reliable.

Recently, it has been pointed out by Krönig that the height of the apices above the shoulder girdle is not constant or always equal. To overcome this difficulty he suggested that the resonant areas above the clavicles be mapped out and these areas compared. A slight change in position (of these areas) is of little consequence, but a difference in size or in the sharpness of their definition is suggestive of disease. Very light and moderate percussion should be employed alternately in mapping them out. It is well to begin on the clavicle and along the border of the trapezius muscle and then to connect these points. Other methods have been suggested, but are not so simple as this.

**Auscultation.**—The first abnormal physical signs in pulmonary tuberculosis are those detected by auscultation, but even these may first occur months after the primary infection. It is hardly necessary to state that the patient should be stripped to the waist and covered, if desirable, by a chest cloth or blanket. Stethoscopic auscultation through the thinnest apparel is exceedingly dangerous both to patient and examiner. Special attention should be paid to the borders of the lungs.

The whole chest should be explored in regard to the vesicular murmur on quiet and forced breathing, provided the patient's strength permits it. He should be made to breathe noiselessly through the mouth whenever loss of vesicular murmur occurs at both apices. This will exclude in some instances a "loss" of vesicular murmur due to exaggerated transmission of the breath sounds from the nasal region due to obstruction. A series of short, quick inspirations often aids in demonstrating a good vesicular murmur in superficial "breathers." A venous hum above the clavicle may be mistaken for a change in the vesicular murmur.

A difference exists between the vesicular murmur on the two sides of the chest, which Dunges believes is independent of the fact whether the patient is right- or left-handed. Some excess of breathing is often present on the right side as low as the level of the second rib and second vertebral spine, and the expiration may be a trifle prolonged. In these regions the vesicular murmur may even have a slightly bronchial quality, especially over the inner part of the first interspace. In persons accustomed to a sedentary life, who

have never breathed properly, the vesicular murmur may be weak on quiet respiration.

Changes may occur in the quality of the vesicular murmur, in the relative duration of its two parts or in its continuity and equality. The first change to be detected is often some harshness and increased loudness. This in most cases is constant increase of loudness or elevation of the expiratory murmur—prolonged high-pitched expiration. Grancher held that the earliest change is a constant weak, harsh, or wavy inspiratory murmur, due to an inflammatory swelling of the lining of the terminal bronchioles, which if sharply defined at one apex is very significant. Wavy breathing precedes weakened breathing, which probably occurs only when the area of infiltration has reached some size. A change in the vesicular murmur is often the only variation from normal found on auscultation. In many cases it is difficult to define this slight change. Some deficiency in vesicular murmur was noted in 82 out of 201 incipient cases. Of 107 cases with a lesion on one side, 39 had some loss of vesicular murmur; of 94 with a lesion on both sides in 43 there was some deficiency in vesicular murmur.

**Wavy, Jerky, or Cogged Breathing.**—Jackson, in 1833, first called attention to the fact that in some pulmonary diseases the vesicular murmur is not continuous, but, as Thompson has called it, "wavy," an adjective since widely used to designate this change in the vesicular murmur. In pronounced cases the breathing is not heard for a time, and reappears and disappears several times in a single respiratory act. This has been termed cog-wheel or jerky breathing. The wavy quality occurs chiefly during inspiration, but at times may be heard in expiration. Wavy or cog-wheel breathing over the site of the lesion does not occur often in early stages, where the lesion is situated at the apex. Wavy breathing may be due to the forced inspirations and heard only when such are taken. Under these circumstances it is usually muscular in origin and has no significance. When confined to one apex, however, it is very suggestive, and a patient with it should always be looked upon with suspicion.

Pathologically, wavy breathing is usually considered due to pressure on and obstruction of the bronchioles by small, scattered foci of disease, change in the pulmonary elasticity, or to pleuritic changes. Williams and Henssen, however, believe that it is connected with the pulse rhythm and is due to hyperæmia or to present or former inflammatory processes. In other words, the increased density results in better conduction of the cardiac sounds, Wavy breathing over both sides is quite frequent in nervous patients and is no indication of disease. It is frequently heard at the base behind, especially on the left side. It was present in 9 of 201 patients in the incipient stage, in 7 on the left, and in 2 on the right. In 3 of these patients a lesion developed later at the site of the wavy breathing. In many cases, however, no further change has ever taken place, and the "wavy breathing" was in some cases undoubtedly a cardiorespiratory murmur.

**Prolongation of Expiration.**—The first change to be detected by auscultation in some cases is a prolongation of the expiration, often slightly raised in pitch, due to a constriction of the bronchioles. In 107 patients in the incipient stage with a lesion on one side the breathing was normal in 26. In the remaining 81 prolonged expiration was present in 29, being the only auscultatory sign in 6. When lesions occurred on both sides (94 cases) prolonged expiration was present on one side in 29 cases, in 8 on both.

**Weakened Breathing.**—Weakened or distant breathing at one apex is often a very suggestive sign. It was present in 10 of these patients with a single lesion; in 1 it was the only abnormal auscultatory sign, and in 6 the only change to be detected on examination of the respiratory murmur. In 94 patients with a lesion on each side, in 10 the breathing was distant. The weakened breathing in these cases was at the site of the lesion or lesions. Weakened breathing may be due to extensive and numerous foci of disease, to pleuritic changes, or to the narrowing of a bronchus by pressure or by mucus which after coughing may be removed. In other instances, however, only after some days is the breathing of normal or increased strength. Feeble musculature causes weakened breathing throughout both lungs.

**Puerile and Harsh Breathing.**—This is also rather infrequent in early stages, and while found frequently on the unaffected side in advanced stages it is by no means an unfavorable sign, as in many instances it indicates compensatory action. In a small number of the incipient cases studied (4), harsh breathing accompanied prolonged expiration. In 107 cases with a lesion on one side, harsh breathing with some loss of vesicular murmur was present in 6; puerile breathing in 6 cases. Of 94 cases with a lesion on both sides, harsh or puerile breathing was present in 28 cases.

The "metamorphosing" breathing of Seitz is applied to that form in which a change in the character of the breathing occurs during inspiration, a change from a high-pitched to a normal vesicular quality, or vice versa. It is said to be pathognomonic of pulmonary tuberculosis, rare in occurrence, and due to a partial and momentary constriction of a bronchus by mucus. In some cases movement of the chest wall begins before the respiratory sounds are audible, which has been termed "delayed respiration," but has no special significance.

When the disease becomes fairly well marked the vesicular quality loses its pure tone and becomes more or less bronchial, the type of breathing most common in pulmonary tuberculosis and spoken of as bronchovesicular or vesiculobronchial breathing.

**Vocal Resonance.**—The vocal resonance often varies directly with the vocal fremitus and, like the latter, is more pronounced on the right, to the level of the second or third rib and third vertebral spine, or even lower on the back. A slight increase on the right is therefore difficult to detect. The whispering voice as well as the ordinary tone should be very carefully auscultated over the entire chest, as small or deep-seated areas of consolidation are often first detected by this means. As the disease advances the vocal resonance passes through various gradations into bronchophony, and when excavation occurs whispering pectoriloquy is a very important physical sign. In the 201 patients in the incipient stage the vocal resonance was noted as normal, *i. e.*, slightly increased on the right in 124. In 77 cases it was increased and corresponded with the lesion in every case but one.

**Adventitious Sounds.**—*Rales.*—It is rare to detect any adventitious sounds in the lungs in incipient pulmonary tuberculosis on quiet breathing. When rales are detected on quiet breathing the case is usually no longer in the incipient stage. Fränkel, indeed, holds that when any rales are heard the disease is no longer in its incipiency. Rales are in most patients in incipient stages heard only during forced inspiration following cough and may not be constant. It is often necessary to explain carefully—best by example—to the patient how to cough in order to bring out clearly any adventitious sounds.

He should be directed to cough with some force as noiselessly as possible and immediately after it to take a full, fairly rapid inspiration, contracting his muscles and moving his shoulders during the whole procedure as little as possible. In certain cases a cough at the end of expiration followed by a full inspiration brings out rales heard in no other way. In some instances the rales are heard only on quiet breathing, in others they disappear after the first deep breath.

All varieties of rales are heard in pulmonary tuberculosis, but fine and moderately coarse ones are the most frequent. Resonant (consonating) rales occur over cavities, but may also be present where no other signs of cavity exist. Gurgling rales indicate either bronchial dilatation or cavity formation. While in early stages only a few fine rales, or a localized rhonchus, whining in character (Turban), heard with difficulty after coughing, above one clavicle, may be present; in advanced stages rales may be so numerous and so loud that the breath sounds are completely obscured. In the early stages rales often occur only during inspiration following cough; at times only at the end of inspiration or even only during expiration after cough. The "mucous click" is common in advanced pulmonary tuberculosis and is said to indicate softening. Moderately coarse rales may be transmitted from one side to the other.

Rales are most frequently heard first above or below the clavicle, slightly more often on the right side. The supraspinous area is often early involved and should be carefully examined. Very often a few rales, fine or moderately coarse, are heard after coughing in the infra-axillary region on the affected side and are considered by some as an auscultatory control of Williams' diaphragm phenomenon. They may persist for some time, and after the diagnosis is made too much importance should not be attached to them. In some instances rales are heard only when the patient is in a reclining position (Stanton, Ransom).

*Pleuritic friction*, except that variety simulating intrapulmonary rales, is rare in early stages, possibly because of the apical location. It was noted in only 2 of 201 patients with incipient disease. Leaming held in 1887 that many adventitious sounds are of pleuritic origin, and thought that subcrepitant rales are produced in the pleura. The question is still a mooted one, but moderately coarse, superficial rales may be heard over the entire chest with absence of all sputum. This can be explained in two ways: first, that the sounds are of pleuritic origin; second, that the exudate is absorbed. In a recent case, in which the patient presented superficial, moderately coarse rales on coughing over the entire side, death was caused by an acute abdominal condition. At autopsy the pulmonary apex was firmly adherent to the chest wall, and a few adhesions bound down the posterior border along the spine. Scattered throughout the lung were fibrous nodules, some of which contained caseous matter.

Creaking and rubbing sounds, believed by many to be produced in the lungs themselves, are difficult to separate from pleuritic friction sounds and deep-seated rhonchi. The pseudopleural rub of Rosenbach, heard at the base between the nipple and the anterior axillary lines, is probably in part muscular and in part due to atelectatic crepitations.

*Cardiorespiratory murmurs* are frequently mistaken for pathological wavy or interrupted breathing. If they occur at the left base with no other signs of disease, any connection with pulmonary disease can be excluded.

The frequency is ordinarily two to four to each inspiration. They rarely occur during expiration. A whiffing systolic bruit, heard chiefly during inspiration along the left border of the sternum, due to the forcing out of air at each cardiac cycle, is not rare. Occasionally a rale is heard synchronous with the cardiac beat, usually on the left front, but at times in the right interscapular region.

Wide transmission of the heart sounds indicates a very forcible beat or beginning infiltration of the pulmonary tissue. If increased cardiac action through nervousness or through cardiac disease can be excluded, it is well at least to think of beginning consolidation. Some accentuation of the second sound over the pulmonic area is frequent in advanced but uncommon in early stages.

*Post-tussive suction*, a peculiar high-pitched, sucking sound occurring during the first part of inspiration following cough, is heard not uncommonly over cavities. It does occur in the chest, however, in which no other signs of cavity exist. The *veiled puff* is a "single, rather high-pitched sound, of a puffing character, which becomes suddenly audible toward the end of inspiration" (Fowler). It is said to be a valuable sign of a small sacculated bronchiectasis, but is rare in pulmonary tuberculosis.

**Roentgen Rays.**—The chief value of the *x*-ray examination is for diagnosis, but it may yield valuable information during the course. It reveals deep-seated cavities, congestion, enlarged bronchial glands, or beginning disease in the opposite lung not discovered by ordinary physical examinations. It thus aids in prognosis. It can hardly be said to repay the study necessary to acquire all the details, and should be relegated to the *x*-ray expert.

**Latent Pulmonary Tuberculosis.**—Physical signs may be entirely lacking in this group of patients, which from the standpoint of treatment is most important. "Closed" pulmonary tuberculosis belongs here—"closed" because tubercle bacilli are not found (ulceration or "opening" of the focus has not occurred). In a majority, however, slight physical signs are present, though taken alone they may not be sufficient for diagnosis. A percussion note a trifle high-pitched and short above the clavicle, a shrinking of the resonant area above the clavicle, lessened diaphragmatic movement on one side, a slight deficiency in the vesicular murmur, and possibly a few fine rales clearing up on coughing are the most common signs. Any one of these may occur alone. In other words, the physical signs in this stage are often simply suggestive and suspicious and indicate further investigation. The so-called "pretuberculous" stage often belongs to this group.

**Early (Incipient) Pulmonary Tuberculosis.**—The physical signs have now become more pronounced; there is lessened movement at one apex, with slight dulness, a few fine or moderately coarse rales, heard in most instances only during the inspiration following cough. The change in the vesicular murmur is more marked and, besides high-pitched prolonged expiration, the inspiration may be changed and bronchovesicular breathing may occur. Wavy or weakened breathing may be present. The vocal fremitus and vocal resonance are both likely to be increased. In other words, persistent signs of local bronchitis at one apex are usually the first positive physical signs, although others are quickly added.

**Advanced Pulmonary Tuberculosis.**—All physical signs to be detected in the lungs may be heard at one time or another in advanced cases. One apex may present very early signs, while the other is in an advanced stage of

the disease. In any case, however, the "physical signs" usually refer only to the most advanced lesion in the lungs. In rare cases either dulness or rales may be entirely absent. Hyperresonance may occur.

**Softening.**—The physical signs of "softening" are very uncertain. An increase in the size of the rales and a metallic quality or ringing character are said to indicate softening as well as the moist or dry crackling. The respiratory murmur may be much weakened and even replaced by two or three clicks during inspiration and expiration following coughing. The condition of the surrounding tissue modifies many of these physical signs.

**Signs of Cavity.**—These depend largely upon its size and location, and the condition of the surrounding tissues. Cavities of fairly large size may be readily overlooked either because a stoppage of the bronchus prevents the entrance of air, or because the cavity is filled with secretion or deeply situated. Unless superficially placed or surrounded by consolidated lung tissue, it is not possible to diagnose cavities smaller than a walnut. Except in acute pulmonary tuberculosis, cavities may be assumed to be present practically always in the last stages, but often are discovered only at necropsy.

Inspection nowise differentiates cavity formation from fibrosis. In some rare instances more local bulging and retraction than is usual occur in a limited area on coughing. The note over a cavity may be normal, dull, flat, tympanitic, or amphoric. Change in tone may occur with change of position (change in position of liquid contents, etc., Gerhardt), with opening (higher note) or closing (lower note) the mouth, *i. e.*, mouth breathing (Wintrich), or with respiration (higher during inspiration), and may disappear if the tension of the wall is very great (Friedrich). Turban believes that Wintrich's and Gerhardt's changes of pitch are the most reliable signs of cavity. Change of position, leading to occlusion of the bronchus by the fluid contents, may obliterate many of the signs of cavity or lead to its diagnosis by emptying the cavity. The cracked-pot note is frequent over superficial cavities with a narrow opening into a patent bronchus situated in the upper lobe anteriorly between the clavicle and fourth rib, and is rare in cavities elsewhere. In a few patients percussion above the third rib and third vertebral spine causes cough, which Erin believes is pathognomonic of a cavity. On auscultation the respiratory murmur may be intense, distant, or even absent, but is usually tubular, amphoric, or cavernous in quality. While auscultating a cavity the cavernous breathing may be quickly replaced by tubular breathing, only to yield in turn again to cavernous breathing. The metamorphosing breathing of Seitz may occur.

Coarse, bubbling rales are most characteristic of large cavities partially filled with secretion. Sharp, ringing, metallic rales are more frequent in smaller cavities, and may be heard only after cough. In old cavities, hisses, creaks, sonorous and sibilant rhonchi may replace all other rales, and in a few cases there may be no rales at all. The metallic tinkling sound occurs but rarely. The veiled or especially the cavernous puff may occur. Post-tussive suction is frequent. Clicks or gurgling sounds may be heard over cavities in the left upper lobe synchronous with the heart impulse. The voice sounds over a cavity are usually much increased, bronchophony practically always occurring. Whispered pectoriloquy, of low pitch and blowing quality, is one of the most trustworthy signs of cavity. The vocal resonance is quite commonly amphoric or cavernous. In cases with a chronic cavity the area of cardiac impulse may be greatly increased, and in some,

instances with cavity on the right side the point of maximum impulse may be as far out as the right nipple line. Hippocratic succussion and the coin sound may be heard over large cavities, and in some instances pneumothorax has been diagnosed. The physical signs of an apical cavity may completely disappear in front and be heard only at the apex posteriorly, or more rarely disappear entirely. A cavity may be overlooked if the patient is not made to cough and so remove a plug of mucus in the bronchus leading to the cavity. On *x*-ray examination cavities if empty and if not surrounded by too thick a layer of diseased lung appear as light areas.

**Signs of "Activity," "Arrest," and "Cure."**—It is impossible to tell from a single examination by the physical signs whether the disease is progressing or retrogressing. The physical signs may suggest great activity when the disease has been inactive for months. The contrary is also true.

Lungs once affected with tuberculosis are seldom if ever "cured" in an anatomical sense. Some patients with incipient disease after a lapse of months present no physical signs, but few of those in advanced stages recover without pulmonary scars detectable by physical examination (*e. g.*, signs of consolidation, emphysema, etc.). It is remarkable what extensive physical signs may be found in patients who have enjoyed years of good health who may go on to apparent cure and remain well for years with no diminution of the physical signs. Most patients present slight retraction of an apex or base, some dulness on percussion and loss of vesicular murmur which may even pass into bronchial breathing. Pleuritic sounds may linger in various regions, but it is still questionable how soon a patient with rales over any extent of the chest can be said to be "cured."

**Myoidema.**—This, first described by Stokes and named by Lawson Tait, occurs in two forms, nodular and fibrillar or fascicular. In the incipient stages myoidema may occur, but is usually absent. It may occur only on one side or more on one side (usually the side affected) than on the other, and may disappear as a fatal termination approaches. "Myoidema seems to be due, apart from mere thinness, which is so important for its production, to an overexcitability of the muscle or its nerves, and it may be either physiological or, as is more usual, an evidence of some nutritive disturbance in the muscle itself, and this may depend on local disease in the muscle tissue, or be part of some general impairment of nutrition" (West). It has little diagnostic or prognostic importance, but when present demands a careful general examination of the patient, especially of the lungs.

**Hippocratic Fingers.**—Clubbing of the fingers with down-curved nails is usually a late manifestation and occurs in cases of long standing, generally with cavity. It is practically never observed in the incipient stage, unless the pulmonary tuberculosis is secondary to some other respiratory disease. Pollock states that it is present in 29 per cent. of males and 23 per cent. of females, or about one-third of all cases. Trousseau thought it developed first in the thumb and index finger of the right hand, next in those of the left hand, and then involved the other fingers in order of size. The toes are often affected, and the nose may be involved. The base of the nail is palpable when the distal extremity is pressed upon.

**Hypertrophic Pulmonary Osteo-arthropathy.**—Since its first description by Bamberger a number of cases have been observed associated with diseases of the chest attended with prolonged suppuration. It is rare in pulmonary tuberculosis, not one instance occurring in about 2000 cases of

all stages of the disease. The small joints of the hands and feet are usually affected, but the wrists, elbows, and rarely the hips and shoulders may be involved.

## THE MODES OF ONSET.

The exact time of onset, except in acute cases, can rarely be definitely determined. In a large majority, signs of failing health long precede symptoms localized in the lungs. Only a careful inquiry brings out these facts, which seem in many instances to have entirely escaped the notice of the patient. For this reason the onset in regard both to time and to symptoms is difficult to determine exactly, and King has pointed out the great discrepancy between the onset described by the patient and the probable onset. Many have at the onset or early in the disease some symptom or group of symptoms which characterizes the disease at first and enables us to divide the onset into several groups, which are not sharply differentiated and often combined.

In a study of the onset in 2000 patients admitted to the Adirondack Cottage Sanitarium it has been difficult to separate the various types in many cases, and symptoms localizing the disease in the lungs have in all doubtful cases been treated as characterizing the type of onset. Pleurisy, even years before other symptoms, has been looked upon as tuberculous and the onset in these cases characterized as pleuritic. The onset has been stated to be hæmoptic only when the hæmoptysis occurred in patients who until that time had enjoyed good health. Under the catarrhal form are included all cases which started with "cold," bronchitis, or "grip." In the malarial onset only those patients are included who had definite chills and fever. Many cases of the disease beginning with malaise which have been diagnosed "malaria" are to be found in the insidious onset. In other words, all symptoms of ill-health which could not be attributed to other definite diseases have been taken to be early manifestations of the pulmonary tuberculosis. The most common form of onset was the catarrhal. Bronchitis was the first symptom noticed in more than half of these. About one-fourth had "colds" at the onset, and about one tenth "grip." The remainder included combinations of these forms. Next in frequency to the catarrhal form was the insidious onset, which was nearly equal in the two sexes. Hæmoptysis as an onset followed closely upon the insidious type, and occurred nearly twice as frequently in men as in women. The other onsets in the order of their frequency were pleuritic, malarial, laryngeal, febrile, gastric, and glandular.

**Insidious or Latent.**—Careful inquiry will often reveal symptoms of slight ill-health preceding for weeks, even months, the so-called "primary" hæmoptysis, pleurisy, or acute febrile attack. The patient begins gradually to run down in health; he tires more easily, has less strength, loses a little weight continuously, and constantly has slight elevation of temperature in the afternoon; his appetite is poor, and, if he lives in certain localities, is told he has a "touch of malaria." Undoubtedly many recover at this stage, which fact throws more obscurity about the recognition of this type of onset. Later, pulmonary symptoms, such as cough, pleurisy, or hæmoptysis, develop and the constitutional symptoms, slight at first, become marked and the patient has emaciation, night-sweats, rapid pulse, and hectic fever. This

latent group would undoubtedly include a large majority of all cases if a careful history were taken. In some instances serious disease in other organs masks the onset of pulmonary tuberculosis. The importance of the recognition of this group cannot be overestimated, for in early recognition lies cure. The succeeding two forms of onset are closely related to the latent type and might be included as subdivisions:

**Glandular.**—Recent research has shown that the bronchial glands may be affected shortly after the cervical, and that tuberculous disease of the bronchial glands is closely associated with—some hold an almost constant precursor of—pulmonary tuberculosis. As a rule, only cases with marked glandular involvement or suppuration should be included in this group. The existence of a few slightly enlarged cervical nodes does not constitute a "glandular" onset.

**Onset following Fistula-in-ano.**—In a number of cases a suspicion of pulmonary tuberculosis is first aroused by the development of an ischio-rectal abscess with a resulting fistula. The lungs on examination are found tuberculous, but in many instances the symptoms were so slight that they drew no attention to the lungs.

**Catarrhal.**—This is unquestionably the most frequent. A large majority of patients give a history of repeated colds, an attack of slight persistent bronchitis, or of "grip," as the earliest symptom. It must not be overlooked that many of these attacks may light up a slumbering tuberculous lesion. In some instances this onset closely resembles an attack of asthma. A history of cough during the winter for several years is not uncommon, and its persistence during the summer may first arouse the patient's anxiety.

**Pleuritic.**—The importance of the pleuritic onset has only recently been fully recognized, though H. I. Bowditch long ago pointed out that one-third of his cases of pleurisy with effusion had pulmonary tuberculosis later. Unquestionably, it is wise to treat all cases of idiopathic pleurisy with effusion as tuberculous, whether the effusion develops insidiously, slowly without pain, or acutely and with pain, whether with or without respiratory distress. The physical signs of intrapulmonary disease in these cases may be lacking, but slight signs at the apex should be conclusive. A long interval may occur between the attack of pleurisy and pulmonary tuberculosis, which suggests the possibility of a later infection. Dry pleurisy at one apex or double pleurisy is almost certainly tuberculous if no other exciting cause exists.

**Hæmoptoic.**—In some cases the first symptom undoubtedly is hæmoptysis, which may occur only once or repeatedly several (in one case twenty-nine) years before other pulmonary symptoms develop or may be followed by constitutional and local symptoms. Physical signs may be lacking at first and the patient may enjoy years of good health before other symptoms appear.

**Laryngeal.**—Tuberculous laryngitis is rarely a primary lesion, but in an important group of cases the laryngeal symptoms, hoarseness, aphonia, pain, and dysphagia, may entirely mask the pulmonary symptoms, not only at first but throughout.

**"Malarial."**—Chills, fever, and sweats at the onset occur in a number of cases. The attacks are usually quotidian and may closely resemble those of true malaria. In some instances the chills and fever occur irregularly and rarely every two or three days.

**Nervous.**—In patients markedly neurotic the nervous system may be early affected by the tuberculous toxin. Acute mania occurs but rarely;

melancholia is more frequent. Neurasthenia is common and may predominate over the other symptoms.

**Febrile.**—Slight but persistent fever is at times the only symptom at onset. In other cases the fever may be pronounced for some days and the patient profoundly prostrated, suggesting in some instances typhoid fever (typhoidal onset). Again, the fever is coupled with chills and sweats and suggests malaria, either quotidian or tertian. The vasomotor and nervous systems are often early affected and easily influenced.

**Anæmic or Chlorotic.**—Severe anæmia or chlorosis with its associated symptoms may be marked at the onset, especially in women, and lead to a diagnosis of a primary anæmia. Murmurs are present in this type, but the circulation is not normal, and loss of weight may not occur while the temperature is usually slightly elevated. Chlorosis has become much less frequent with more exact methods of diagnosis of pulmonary tuberculosis.

**Gastric.**—Loss of appetite, nausea, some vomiting, great discomfort after eating, distention or an acid dyspepsia with eructations, may be the only symptoms for a longer or shorter period. It is not infrequent for patients to have gastric lavage performed even after hæmoptysis, so pronounced may be the gastric symptoms. Emaciation is more rapid than is usual in simple dyspepsia, and the symptoms frequently disappear when the pulmonary tuberculosis is treated.

**Diarrhœic.**—The onset with diarrhœa, while not common, is often well marked. It rarely precedes expectoration and slight cough, but predominates all other symptoms. In some cases the swallowed sputum causes an early intestinal tuberculosis, which may be the chief symptom throughout, but more often a catarrhal enteritis is set up. This form of diarrhœa may continue for months and the patient lose but little weight.

**Typhoidal.**—Acute tuberculosis of the lungs may so closely simulate typhoid fever that the pulmonary disease may be overlooked for weeks. Such on onset is by no means rare, and the disease, while usually acute throughout, may become subacute, chronic, or even undergo arrest.

## THE COURSE AND DURATION.

**Course.**—The primary seat of pulmonary tuberculosis is practically always near the apex of the lung, and as the disease progresses the lesion extends downward. In the more chronic and fibroid cases a definite course, first clearly described by Fowler, is often pursued, but in the acute and caseous forms the disease may spread directly from lobe to lobe. The three most frequent sites of the primary lesion are (1) just above or below the clavicle, 1½ inches below the summit, rather nearer to its external and posterior borders, (2) the supraspinous fossa, and (3) the first and second interspaces below the outer third of the clavicle. In a study of 201 early cases at the Adirondack Cottage Sanitarium the physical signs were found first at the apex anteriorly (supraclavicular fossa and first interspace) in 56 and posteriorly (supraspinous region) in 21 patients. The disease began 28 times in the supraclavicular, 5 times in the subclavicular fossa. In 36 cases it was impossible to decide whether the first signs appeared above or below the clavicle. While the disease began more frequently on the right, the primary localization was the same on each side.

When the disease begins above or below the clavicle, its usual course of extension is first to the apex posteriorly, then downward along the sternum and along the spine as far as the apex of the lower lobe (to the level of the third or fourth vertebral spine). The entire upper lobe is then involved, but even before this occurs the apex of the lower lobe (opposite the fourth and fifth vertebral spines) may be affected. The coexistence of a lesion at this spot and at the apex, even if slight, is almost positive proof of tuberculosis (Fowler). The physical signs may then quickly extend to the base, where for some time a few rather superficial rales, chiefly in the infra-axillary region, may have existed. The signs in the apex of the lower lobe may clear and the patient coming under observation is thought to have a basal affection, due possibly to a different cause than that of the apical lesion. The apex of the opposite lung is, Fowler thinks, usually affected after the apex of the lower lobe on the same side; but there are numerous exceptions to this course, and it is not infrequent to have a few signs develop at the opposite apex just as the signs at the apex primarily affected disappear.

The disease in the second lung follows the same course as in the first. In the majority of instances the diseased area is not continuous, but consists of scattered nodules with healthy areas intervening.

If the disease begins posteriorly the apex of the lower lobe is usually more quickly affected. Otherwise, the course is similar to the foregoing. The lesions in most cases are, according to Fowler, much more advanced posteriorly than anteriorly. This is not by any means always the case. Fowler's third primary seat under the outer third of the clavicle is of rare occurrence, and the disease is said to spread downward to the interlobar septum. When the apex of the lower lobe is affected the signs may not extend downward parallel to the spine, but along the border of the outward rotated scapula (the position it assumes when the hand is placed on the opposite shoulder and the elbow elevated). According to Fowler this assumes a wedge shape, but this, however, in many cases cannot be demonstrated clinically.

When the opposite side has become involved an area of tubular breathing with whispering bronchophony and resonant rales is frequent in the third and fourth interspaces just outside the nipple line. The physical signs often simulate those of cavity, but later in many cases the only physical signs remaining are a few fine rales. While frequent on the left side, this condition is rarely met with on the right, and may in some cases be the first point affected on the opposite side. Williams thinks the right lung more prone to secondary infection from the left than the left from the right.

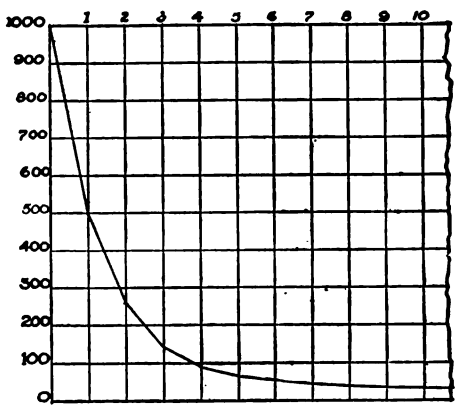
In a few cases the apex of the lower lobe is the first part of the opposite side to be affected. This may be due to a secondary infection, in which cases the lesions assume bizarre locations. Basal lesions usually mean a secondary infection from an undetected primary focus or an overwhelming primary infection. The disease usually quickly advances in the latter case to excavation, and infection of the opposite side occurs early. The incipient stage of pulmonary tuberculosis may last but a few weeks, but on the average may be said to extend over several months (up to six) and in a few instances may last for years. Some patients who have made perfect recoveries from an advanced stage of the disease may be later found to present signs of incipient disease on relapse.

The vulnerability of the apices has been attributed to the fixity of the upper

chest, diminished functional activity, and consequent lessened resistance; to the limited aëration of the apical air cells and bronchi, which are therefore more easily choked with debris; to early calcification of the first costal cartilage, with the consequent limitation of movement; to supposed abnormalities or imperfections of the circulatory conditions at the apex; to the thicker bronchial secretions, owing to the relative dryness of the apices from the subsidence of the blood, the effect of gravity (Rindfleisch); to the fact that from the standpoint of comparative anatomy the apices are the most unstable parts of the lungs (W. Hutchinson); to the greater exposure of the upper part of the lungs to the influence of cold air, and, lastly, as Colbeck and Pritchard have pointed out, to the fact that the apices extend (1½ inches) above the bony cage of the thorax, that they depend for support upon the position of the shoulder girdle, especially the clavicle, and upon the development of the related muscles. The apices, they hold, are inflated during expiration, and as a result a neutral zone is formed under the first rib 1½ inches below the apex, where foreign particles would most likely lodge. Expiration would drive these substances farther in. The right apex, rising higher than the left, is still more susceptible for the same reason. Lessened functional activity, whatever its cause, is the most plausible reason.

**Duration.**—Pulmonary tuberculosis may last but a few days or extend over sixty or more years; the majority of cases, however, run a chronic or subacute course, with more or less frequent acute attacks. The average duration of the acute cases is between three to six months, but many die in less than four weeks, due, West thinks, to a complicating acute lobar pneumonia. For all cases, acute, subacute, and chronic, the duration may be said to approximate three to four years, while for the chronic it is over twice as long.

FIG. 12




Proportions of dead and living, of all persons dying from pulmonary tuberculosis: 1, 2, 3, etc., years after onset of the disease, based on State, municipal, and private records of death.

NOTE.—The curve follows approximately a straight line after ten years and falls to the base line at forty-one years, the longest duration among the records used being forty years.

A study of the duration of the disease from the deaths occurring in the first 1000 cases at the Adirondack Cottage Sanitarium shows that in patients admitted in a far-advanced stage the disease had a duration of a little over four years; for those in a moderately advanced stage, between five and six years; while for those in an incipient stage the duration was about eight years. Modern treatment has unquestionably greatly prolonged the duration, and this fact may be held to account in part for the decreased tuberculosis mortality of recent years. Acute tuberculous pneumonia and bronchopneumonia usually last from eight to twelve weeks. From a study of recent statistics (compiled by E. G. Pope), Fig. 12

has been constructed. This shows that about 35 per cent. of all patients die in six months, 50 per cent. in one year, 91 per cent. in four years, and 3 or 4 per cent. live from ten to forty years. Sex seems to exert no influence upon the curve.

**Pulmonary Tuberculosis at the Extremes of Life.**—Long recognized as common in children, the frequency of pulmonary tuberculosis has often been overlooked in the aged. The difference in the course of the disease from that in the adult is marked. "In the aged," says Pollock, "systemic disorder, rarely very high, does not find a machine working at extreme pressure, but rather at slackened speed; in the young the whole energy of the animal is being devoted to nutritive action when the disturbance occurs, and the resulting disarrangement is proportionate to the importance of the operations interfered with."

**In Children.**—Pulmonary tuberculosis in children is of frequent occurrence and much more common during the first year of life. Louis' law, that when a caseous focus occurs in the body the lungs are found to be practically always tuberculous, does not hold in children, as Barthez and Rilliet's figures show that in 28 per cent. of cases of tuberculosis in children the lungs escape. Henoch, however, would substitute "bronchial glands" for "lungs" in this law, which he would then uphold. If the symptoms of tuberculosis continue until death the lungs are always affected.

In a large proportion the disease first attacks the bronchial glands whose early involvement and the patency of the lymphatics aid in generalization and prevent localized inflammation and the resulting fibrosis, a condition characteristic of pulmonary tuberculosis in children up to the age of six or seven years. The younger the child the more diffuse is the disease, as a rule, while in older children it is more nearly similar to that in adults. The localization of the disease primarily at the apices is not present in children, but is often most marked in the upper lobe, about the hilus of the lung. Still, however, believes that pulmonary tuberculosis in the child as well as in the adult has a tendency to occur just below the apices of the upper and lower lobes.

Acute processes predominate in these cases in early childhood and several distinct forms can be recognized. A latent form in which the only symptoms are emaciation and fever is not rare and pulmonary signs may occur, but only shortly before death. The pneumonic (lobar) form is rather rare, but the bronchopneumonic form is of frequent occurrence. The pneumonic and miliary forms may differ little from the same types in the adult. The bronchopneumonic form may closely simulate simple bronchopneumonia, and if the sputum, obtained by a swab from the pharynx if necessary, the stomach contents, or the fæces contain no tubercle bacilli the diagnosis may present many difficulties. Expectoration is rare under seven and hæmoptysis under five. Pleurisy and night-sweats are not frequent. The spleen may be enlarged and intestinal infection is common. Genital tuberculosis is rarer than in the adult, but meningeal complications more frequent. Death may occur in one to three weeks in the acute, but the more protracted cases may last from one to three or even six months. In some instances the child may become suddenly ill while teething or during convalescence from fever. There is then a rapid rise of temperature and signs of consolidation; death may follow in a few days (Osler).

Chronic tuberculosis, rare in children under five and not at all frequent

until ten or twelve, runs also in unfavorable cases a shorter course than in adults. In many children a remarkable tendency to recovery is often manifested and under sanatorium treatment children as a rule do better than adults. The physical signs are often misleading and nearly all the classical signs of excavation may be present with consolidation. The wide extent of the signs, however, may arouse suspicion. Cavity formation is rarely recognized under three years, but where the disease exists until death, cheesy nodules centrally situated with softened centres are common, but rarely communicate freely with the bronchi. After the age of eight, signs of cavity differ little from those of the adult. Death usually takes place from the occurrence of one of the acute forms of the disease, from meningitis, or from simple acute bronchopneumonia.

**In the Aged.**—Senile pulmonary tuberculosis, in marked contrast to the infantile type, is characterized by a slighter tendency to generalization, a marked production of fibrous tissue, and a lessened tendency to degeneration. The disease runs often a very chronic course and may be discovered only by accident in the course of what was thought to be chronic bronchitis, emphysema, or asthma. The examination of the sputum may alone establish the diagnosis. An acute course, however, is not rare, and Prus thinks that this form is more common in females. Fever is usually slight or absent in the more chronic forms, cough frequent, and expectoration abundant.

**Termination.**—This may be in cure, arrest, or death. The use of the word "*cure*" in this connection has met with many opponents, and in the sense of a *restitutio ad integrum* is certainly misleading. The inexorable test of time proves that many "cures" are only "arrests," and at least two years should elapse before the patient is said to be more than *apparently* cured. "Healed" has much to recommend it.

In a large majority of the cured patients some physical signs persist. Patients who recover without any persisting physical signs are chiefly those whose lesion is very slight or is so deeply seated that it presents at no time physical signs, the diagnosis being made from the sputum. The majority of cured patients have usually collapse above or below a clavicle or flattening elsewhere, slight dulness, some change in the vesicular murmur (weakened, rough, or even slight bronchial breathing), possibly increased vocal fremitus or resonance, and in many cases a few fine rales, arising in some instances in the pleura. These signs may persist for ten to fifteen years after the patient has resumed his usual occupation in his home climate. Cough and expectoration may not entirely cease, and in many cases where they do the patients are subject to bronchitis. The sputum, however, if present should contain no tubercle bacilli for at least two years. Capacity for work is no criterion of cure, but subjective well-being is important. Kurlow's experiments show that as long as caseous material is present in the lesion, viable tubercle bacilli may occur and a cure is not accomplished. Cavities of any considerable size rarely if ever completely close, but it is not unusual for the physical signs of excavation to become less marked and finally entirely disappear.

**Arrest.**—Pulmonary tuberculosis in the vast majority of cases can never be said to be even "*apparently*" cured. Few chronic cases, however, progress so steadily that they cannot be said to be "arrested" at some time in their career, and in acute cases the first step toward arrest is when the disease becomes chronic. These arrests, however, are frequently only temporary. Arrest can occur when all hope is seemingly past, and every physician with

any experience can recall the arrest and even cure of one or more patients whom he has pronounced hopelessly ill. In fact, in some instances a self-limitation of the disease is strongly suggested. In a small number of cases, especially those with marked fibroid changes, arrest and a condition of asthma seem to go hand in hand.

**Death.**—The majority of patients with confirmed pulmonary tuberculosis die sooner or later from the disease or from one of its complications. Death by asthenia is the most common form (Lebert, 63 per cent.). Death from asphyxia forms 14 per cent. of all deaths (Lebert); it is more common in acute miliary and pneumonic phthisis than in chronic pulmonary tuberculosis. It may rapidly follow an acute exacerbation in a patient previously doing well. Sudden death occurs in a small percentage of cases, where at postmortem no gross lesion sufficient to account for it can be found. Nocard has observed the same phenomenon in animals injected with an overwhelming quantity of tubercle bacilli.

Death from complications occurs in many cases. Of these hæmoptysis is not infrequent (2 per cent., West). Death may be almost instantaneous from loss of blood or from asphyxia, or follow in a short time after repeated hæmoptyses from exhaustion. This form of death seldom occurs in the early stages and rarely follows immediately upon sudden exertion. Syncope is an unusual form of death and occurs most often after pneumothorax, which is the cause of death in 1 per cent. of cases (West). Empyema is rarely the cause of death, and when present usually follows pneumothorax. Death with cerebral symptoms is not uncommon. Meningitis (the cause of death in 8 per cent., West) may develop and run its usual course. In other cases slight paralysis and aphasia may occur one day, last but a few minutes, and death with symptoms of cerebral pressure occur on the following day. Other rare causes of death are intestinal perforation and peritonitis, and thrombosis or embolism of the pulmonary arteries.

Out of about 2500 patients who have been at the Adirondack Cottage Sanitarium, 938 are known to have died, a few in the institution, the vast majority from two to eighteen years after leaving. The cause of death has not been learned in 256 and in 3 the cause was doubtful. Five men met a violent death. Of the 352 remaining males, 322 (90 per cent.) were said to have died of pulmonary tuberculosis, 8 of tuberculous meningitis, 2 of nephritis, 2 of frank pneumonia, and 1 each of pneumothorax, Addison's disease, typhoid fever, diphtheria, appendicitis, intestinal obstruction, pyæmia, and alcoholism. Of 323 female patients, 308 (95 per cent.) died of pulmonary tuberculosis, 3 of tuberculous meningitis, 2 of frank pneumonia, and 1 each of heart disease, nephritis, tuberculous disease of the hip, tuberculous nephritis, appendicitis, pulmonary embolism, cancer of the stomach, postoperative shock, peritonitis, and uterine hemorrhage following abortion. These figures, however, are not of great value.

## THE CLINICAL FORMS.

It is difficult to separate the acute forms from the chronic processes and subacute forms are recognized. An acute onset is not infrequent in chronic cases. The classifications are numerous. Some are based upon clinical data alone, others upon pathological findings, but the most satisfactory take both into consideration.

Classifications have been based upon the origin of the disease (hereditary, congenital, or acquired); upon the temperament of the patient (erethismic or torpid); upon the age (infantile, developmental, adult, and senile); upon dyscrasias (gouty, scrofulous, diabetic, alcoholic, luetic, hysterical); upon the ease of diagnosis (latent, larval, manifest); upon the onset (catarrhal, anæmic, dyspeptic, pleuritic, hæmoptic, febrile, nervous, dyspnœic); upon the course (active and stationary and progressive; remitting, intermitting, and retrogressive; acute, subacute, and chronic); upon the extent of the lesions (circumscribed, disseminated, more diffuse; or incipient, limited, moderately extensive, and advanced); upon the pathological changes (consolidation, softening, cavity formation; germination, conglomeration, softening, cavity formation; or parenchymatous, interstitial, bronchitic, and postpleuritic forms); upon the degrees of susceptibility (decided, yielding, or lost organic resistance); upon the secondary infections (pure tuberculosis, stage of mixed infection, or phthisis); in part at least upon prognosis (phthisis incipiens, confirmata et desperata).

The following classification has been used in this article:

I. Acute miliary tuberculosis.
II. Acute pulmonary tuberculosis.
    1. Pneumonia.
    2. Bronchopneumonia.
III. Subacute pulmonary tuberculosis.
IV. Chronic pulmonary tuberculosis.
    1. Chronic ulcerative pulmonary tuberculosis.
    2. Fibroid phthisis.

I. **Acute Miliary Tuberculosis.**—To many there is an appearance of mystery in the manifestations of miliary tuberculosis; it is set apart as something quite different from the more common chronic forms. If, however, comparative conditions in other infections are kept in mind this difficulty is not so great. If the relation of local infections with a pyogenic organism to pyæmia be considered, we have some basis for the explanation of this form of tuberculosis. Hence, it may be considered as an acute, general infection, usually showing signs analogous to those of septicæmia. The special features in any particular case may be very various and depend both on the acuteness of the infection and the distribution of the bacilli. Thus, if the bacilli enter the venous circulation they will reach the lungs especially, if into a pulmonary vein they will be distributed through the general circulation, and if into the portal circulation they may be deposited in the liver. In the great majority of cases the general infection is secondary to a primary focus somewhere in the body. Primary, general miliary tuberculosis may occur, but must be very rare; infection through the tonsil, for example, may be possible.

Given a local focus of tuberculosis there is always the possibility of this infecting the blood stream and so setting up a dissemination of the tubercle bacilli throughout the body. When we consider how many local lesions there are, the wonder is not that miliary tuberculosis occurs, but that it occurs so rarely. But this general dissemination gives a totally different picture from that of the sum total of a number of local lesions. A patient may have tuberculous disease of many organs, but the results are quite different if these same organs are concerned in miliary tuberculosis. Some would consider it as an infectious disease with the bacilli carried throughout the whole body, rather than as only a general distribution of tubercle bacilli.

It is evident that the clinical picture may vary greatly, depending on the severity of the infection and the special distribution of the bacilli.

**History.**—Von Manget (1700) observed what was perhaps general miliary tuberculosis, but to Bayle (1810) probably belongs the credit of the first description of it. He noted that the tubercles had an equal development throughout the body. In some of the older works the term "granulations of Bayle" is employed as a synonym for miliary tubercles. Of course, by none of these was the essential nature of the process understood. The first accurate description of miliary tubercles in the meninges was given by Robert Whytt, of Edinburgh, 1768, who described them under the heading of "Dropsy of the Brain." In 1798, Sir Astley Cooper described tubercles of the thoracic duct. In 1832 and 1833, Gerhard, of Philadelphia, made an important contribution to the knowledge of meningeal tuberculosis.

The modern conception of the condition dates from Buhl (1856), who held that miliary tuberculosis was a specific infection depending on the presence of a previous focus of tuberculous disease. This was supported by the work of Weigert, who proved the association of miliary tuberculosis with tuberculosis of the bloodvessels.

**Etiology.**—In the majority a previous focus of the disease in the body must be regarded as essential, although infection through the tonsils or by way of the cribriform plate of the ethmoid may be possible; these must be regarded as unlikely. The most frequent lesion is in the lungs (given as 50 per cent. by some observers; it is said to occur in 3 per cent. of all cases of pulmonary tuberculosis). Glandular tuberculosis probably comes next in frequency, and then joint, bone, genito-urinary, and pleural lesions.

Of exciting causes the acute infectious probably take first place, especially measles and whooping-cough. Typhoid fever is held by some to have an important influence, but the chances of incorrect diagnosis should be kept in mind. Trauma, operations, especially upon the bones, pregnancy and debilitating conditions, are all at times of importance. Occasionally, it has followed the rapid absorption of a pleural exudate. In patients suffering from chronic maladies, such as arteriosclerosis and nephritis, a terminal acute miliary tuberculosis is not uncommon.

*Age and Sex.*—Age has an important influence. The largest number of cases occur in early life, especially of the meningeal form. Sex appears to have no influence.

**Incidence.**—This is difficult to give. Among 1440 cases of tuberculosis of all kinds in the medical service of the Johns Hopkins Hospital in eighteen years there were 60 diagnosed as acute miliary tuberculosis, of which 29 were of the meningeal form. Among the 1440 cases, 980 were of pulmonary tuberculosis. This does not give any idea as to the percentage of occurrence of miliary tuberculosis in pulmonary tuberculosis, as in very few did the general symptoms appear while the patient was in the hospital. There were 43 cases of generalized miliary tuberculosis among 417 autopsies, at the Royal Victoria Hospital, Montreal (J. McCrae), on individuals who had some form of tuberculosis. The lungs were involved in 41, glands in 35, spleen in 28, liver in 27, kidneys and meninges each in 21, adrenals in 10, brain (tuberculous tumor) in 6, and in 28 one or more serous surfaces. The thoracic lymph nodes were affected in 33 and the abdominal in 18 of the series.

It is convenient to consider the disease under two forms: first, that in which

the general features predominate, the general or typhoid form, and, secondly, those in which local symptoms dominate. Under the second the most common are the pulmonary and meningeal forms, although others have been described, depending on the predominance of signs in one system, as, for example, the pleura or peritoneum. It must be remembered that these divisions do not always hold and that some show features of two of them.

**General or Typhoid Form.**—The picture is that of an acute general infection without any marked local signs. The onset is usually gradual, with great malaise, headache, anorexia, and perhaps cough, chills, and digestive disturbances. With this there is fever and often an increase in the bronchitis. The temperature is usually irregular, and there may be intermissions of two or three degrees. The irregularity may be varied, the temperature being elevated fairly constantly for some days, and then showing marked remissions. Persistent high fever is usually seen in very acute cases without much involvement of the nervous system. In some the temperature may fall to normal or even below it at one period of the twenty-four hours. An inverse type of fever is occasionally seen and rarely the course is afebrile. As the disease progresses emaciation becomes marked, there may be delirium, the tongue is dry, the pulse rapid but rarely dicrotic, and the picture is one of severe toxæmia. The nervous symptoms are usually marked; restlessness, delirium, subsultus, and hyperæsthesia may be present, with more tendency to dulness and coma. Choroidal tubercles may be present. The respirations are usually increased in frequency and the bronchitis becomes more severe. Dyspnœa and slight cyanosis is common and may be present without any marked involvement of the lungs. Cheyne-Stokes breathing may be present late in the course. The pulse rate is usually high and the heart sounds become feebler, with the first much like the second. Anorexia is usually present and occasionally vomiting. There may be diarrhœa and intestinal hemorrhages. Meteorism is not uncommon and the spleen is usually enlarged. Tubercle bacilli can often be obtained from the blood drawn from the spleen, although this is not a procedure to be advised. The urine contains albumin and the diazo reaction is often present. The blood usually shows a leukocytosis and tubercle bacilli may be obtained in cultures. Occasionally there is a hyperæmic rash, sometimes in the form of small spots, which may simulate the rose spots of typhoid fever, but it does not come out in crops. Late in the course petechiæ may appear, especially about the wrists.

As the disease progresses the symptoms of the pulmonary or meningeal form may become more marked. The course is usually progressive without any period of improvement. The average duration is about four weeks, with usual limits of one to six weeks.

*Diagnosis.*—This may present difficulty in the distinction from any severe infection, but the diagnosis from typhoid fever must be considered as the most important. Miliary tuberculosis is more likely to be regarded as typhoid fever than the reverse. The obtaining of typhoid bacilli from the blood, urine, fæces, etc., and the Widal reaction are most important. The temperature curve is usually more constant in typhoid fever; remissions are more marked in miliary tuberculosis. Dyspnœa and cyanosis are usually more evident in miliary tuberculosis. The presence of typical rose spots is of course important. The spleen may be enlarged in both, although more frequently in typhoid fever. Leukocytosis is more common in miliary

tuberculosis, and the large relative increase in the mononuclears present in typhoid fever is not found. The result of lumbar puncture may be of help, as either typhoid or tubercle bacilli may be found. The finding of choroid tubercles may give the diagnosis.

*Treatment.*—This can only be symptomatic, and it seems hopeless to influence the disease by any therapy.

**Pulmonary.**—In this the pulmonary symptoms predominate and may be severe from the beginning. The picture may vary, depending on the relative severity of the general toxæmic symptoms and the condition in the lungs. The onset may be sudden, occasionally with chills, and the temperature rises to 102° to 104°. It is usually irregular and an inverse type may be seen. In patients with previous marked tuberculous lesions the fever may increase gradually. The disease usually begins with the symptoms of acute bronchitis, or in children those of bronchopneumonia. There is shortness of breath and a dyspnœa quite out of proportion to the physical signs. It has been suggested that this may be due to irritation of the vagus by tubercles. There are occasionally asthma-like attacks, and sometimes Cheyne-Stokes breathing. The cyanosis is usually very marked and may be intense. There is considerable cough with expectoration, which is usually seropurulent or mucopurulent, and sometimes even rusty. In a few instances hæmoptysis has occurred.

On examination, inspection may show good expansion with full interspaces. Percussion usually gives a full note, which may be quite hyperresonant, especially over the anterior margins of the lungs. In some cases the hyperresonant note is obtained over certain areas; this is especially the case in children if there is some bronchopneumonia. On auscultation the breath sounds are harsh, but may be almost obscured by the adventitious sounds. These are usually heard everywhere, and at first fine, often very intense, crackling rales predominate. Fine crepitations have been thought to be due to tubercles on the pleura in some cases. There may also be sonorous and sibilant rales, while with the progress of the condition the rales may be coarser and moister. If there are areas of bronchopneumonia, tubular breathing may be heard over them. In case there has been a definite tuberculous lesion in the lung before, the usual signs are heard over this. The sputum may contain tubercle bacilli, possibly from the primary focus, if this be pulmonary. Only in the more chronic cases can they come from breaking down of the miliary tubercles.

The pulse is rapid and feeble. The heart sounds are clear, but may be obscured by the rales. Choroid tubercles have been found. The spleen is usually enlarged. The course of this form may be rapid, but in some the process may become more chronic and last even for months.

The *diagnosis* may offer no difficulty. In some the absence of any definite physical signs, the association of rapid breathing, dyspnœa, and cyanosis, excites suspicion. In some cases of bronchopneumonia, especially in children following one of the acute infections, it may be difficult. In some instances lobar pneumonia may simulate this disease, but careful examination should prevent error. In bronchitis occurring in elderly people, especially with marked emphysema, there may be difficulty for some days. The intense bronchitis of typhoid fever, especially if associated with early severe toxæmia, may cause confusion, but other signs are likely to make the diagnosis clear.

**Meningeal Form.—Tuberculous Meningitis.**—*Etiology.*—In the majority this is secondary to tuberculous disease elsewhere, although in a few it has been suggested that it is primary in the meninges. The acute infections are important factors in determining the onset. In some instances the onset may be associated with trauma.

*Age.*—This form usually occurs in young children below the age of four years, although it may be at any age. In a series of 52 cases studied by Koplik,[1] 11 were under one year. The average age was a little over four years. The age in 100 cases in children collected by Still showed in the first year 13, from the second to fifth year 70, and from the fifth to the tenth year 17. Of 126 cases between the ages of sixteen and sixty (Scitz), 47 were between sixteen and twenty-five, 50 between twenty-five and forty, and 19 between forty and sixty. The bodily condition has no special influence, except that an existing tuberculous lesion may have caused some departure from sound health. In some instances the meningeal involvement is associated with miliary tuberculosis elsewhere.

*Onset.*—In the great majority this is gradual. If the disease follows one of the acute infections the conditions may merge into each other, or previous ill health may have been due to an existing tuberculous lesion. In 86 per cent. of Koplik's series the onset was gradual. There is usually a history of the child not having been as well as usual, or perhaps there was loss of weight, irritability, anorexia, lassitude, and restlessness in children, and in adults a change in disposition, headache, and malaise. The symptoms of a gradual onset may be present for some weeks. Occasionally, older children and adults may show slow cerebration, perhaps with some affection of speech. In some instances the history may be of sudden onset, with fever, chills, vomiting, and perhaps convulsions, but this is rather exceptional. An injury may apparently be the determining factor.

The course has been usually described in three stages: (*a*) *The stage of irritation.* In this there is fever, which is often remittent, headache, vomiting, and perhaps convulsions. The child may be restless and much disturbed by twitching of the muscles. The headache may be very severe, and in a child the hand is often put to the head with the utterance of an unusual cry. This is a curious sound, often very characteristic, which has been called the hydrocephalic cry. Some patients scream constantly except when under chloroform. Vomiting may occur, but is not often very persistent. The bowels are usually constipated. There may be some rigidity or stiffness of the neck. The pupils are usually contracted. The pulse is generally rapid at first. (*b*) *The stage of cerebral pressure.* The temperature is variable. The initiative symptoms become less marked; the child is dull, difficult to arouse, and may be delirious. Retraction of the head becomes more marked. The pupils are dilated, and there may be ptosis or strabismus. There may be monoplegia or hemiplegia; in others there is rigidity of one side of the body. There may be convulsions. Vomiting may occur, and constipation is common. The abdomen is retracted, or, as it is often termed, carinated. The pulse is slow and at times irregular. The respirations are slow and sighing. Cheyne-Stokes breathing may appear. Various skin lesions are common, such as erythema and herpes. (*c*) *The stage of paralysis.* The coma increases and the patient is quite oblivious to the

[1] *Journal of the American Medical Association*, 1907, xlviii, p. 1149.

surroundings. Convulsions, either general or local, occur, and there may be paralysis of certain muscles. The pupils are dilated; optic neuritis and paralysis of the ocular muscles may occur. Diarrhœa is common, with incontinence of the urine and fæces. The temperature is variable, and may rise to 105° or 106° or fall to subnormal, 94° or 95°.

It is not always possible to recognize these stages. The symptoms show so much variation that they are only more or less general and not necessarily sharply marked off. The patient usually lies persistently on one side, with the legs flexed on the body, and resents any attempt to alter this.

*Nervous System.*—The mental state, except in the early stage of irritation, is usually dull and apathetic. The patients pay little attention to what is going on around them. As the disease progresses the patients may become unconscious, but often it is more a state of stupor. Occasionally a patient who has been comatose arouses for a time and may be quite conscious, only to relapse into coma. Hyperæsthesia, so common in the epidemic form of meningitis, is usually absent. Pain in various parts of the body or limbs may be complained of by older patients. Headache is complained of by adults; in children its presence may be suspected by the crying and the movements of the hand to the head. Convulsions are often present at some stage or other. There may be irregular tetanic contractions of one extremity. Tremor may occur, and in some irregular movements are common. Curious associated movements may be seen. Some patients suck the lips or have repeated motions of the jaws. If paralysis occurs it is usually hemiplegic or monoplegic. There may be facial paralysis. In the eyes the third nerve is most frequently involved; in some cases this may be with paralysis of the face, limbs, and hypoglossal nerve of the opposite side. General convulsions may occur at any stage; local spasms are common, and may vary in situation from day to day. They may be followed by paralysis.

*Kernig's Sign.*—This is by no means constant and was found in only 22 of Koplik's 52 cases. In this series the Babinski reflex in children over two years of age was more useful, being present in 23, and, if found, Koplik considers it an important aid in the recognition of the tuberculous form. The general reflexes are usually present until the later stage, when they disappear. Rigidity is present in the neck in the majority; it was absent in 14 of Koplik's 52 cases. It does not usually appear as early as in the epidemic form, and generally does not cause such marked retraction of the head. It may occur in the extremities. *Paresis* of the muscles usually comes on late in the course. There may be great variation in this condition from day to day.

*Lumbar Puncture.*—This usually gives results of the greatest importance. The fluid may be hazy, turbid, and under considerably increased pressure. Rous[1] in thirteen tests found a mean pressure equal to 308 mm. of distilled water (the normal is 120 to 180 mm.).

The protein content of the fluid is usually increased and may average 1 gram per liter. In some cases there is a substance present which reduces Fehling's solution. The most important point is the presence of tubercle bacilli. It may be said that the number of cases in which tubercle bacilli are found in the spinal fluid is directly proportional to the care with which

[1] *The American Journal of the Medical Sciences*, 1907, cxxxiii, p. 567.

they are sought. The fluid should be obtained free from blood, centrifugalized for a considerable time, the sediment stained and long search made in the prepared slides. During one period tubercle bacilli were found in 24 out of 27 cases observed by Koplik. The fluid may be injected into guinea-pigs, which is certain, but slow.

*Cytology.*—As a rule, the total number of cells is much increased. The most striking finding is the large percentage of mononuclear cells (usually over 90 per cent.). In rare cases the polymorphonuclear leukocytes may predominate, but no rule can be laid down as to any special significance in this. Aside from the presence of tubercle bacilli and a large percentage of mononuclear cells, the other information obtained by lumbar puncture may be regarded as rather more valuable in excluding tuberculous meningitis. When the pressure, amount of protein, and the cellular elements are normal, these must be regarded as being strongly against tuberculous meningitis.

*Percussion of the Skull.*—Koplik has drawn attention to the importance of Macewan's sign in the recognition of internal hydrocephalus in young children. He found it present in 34 of 52 cases. In doing this the patient should be upright, with the head slightly inclined to one side, the skull being percussed over the pterion. The obtaining of a tympanic note speaks for the existence of internal hydrocephalus. This sign may apparently be present comparatively early in the course.

*Eyes.*—Ptosis and strabismus may occur. The pupils are usually contracted in the early stages, but as the disease progresses become dilated, and toward the end may give no reaction to light. In some cases an oscillation of the pupil between contraction and dilatation is seen. The changes in the fundus are important. The disk may be swollen, with indistinct margins, the veins distended; or there may be optic neuritis, which is usually present in the latter part of the course. In two-thirds of Koplik's cases there was some change in the disk. The presence of choroid tubercles is the most important finding. The reports as to the frequency vary greatly, some observers having failed to find them in a number of cases. In 9 among 46 of Koplik's series they were found in the second day of active symptoms, so that they may apparently appear at any stage of the disease.

*Temperature.*—As a rule, with the meningeal involvement the temperature is low. It may rise shortly before death or become subnormal. *Vomiting* is variable and after the onset may occur for several days and then cease. The *pulse* may show early irregularity. During the stage of irritation it is often slow and later again becomes rapid.

*Duration.*—This varies greatly. There are some cases, most often seen in adults, with a very rapid course, the acute features lasting only a few days. On the contrary, the duration may be prolonged, the condition becoming one which might almost be termed chronic meningitis. This is especially likely if the meningitis be limited, when psychical symptoms or these suggestions of brain tumor may predominate. The average duration may be stated as between three and four weeks. In some instances there are periods of improvement followed by relapse. In some of these cases the improved condition may be so marked that doubt is cast on the diagnosis, unfortunately only for a short time. In some the course is almost latent and the duration may be impossible to state.

*Diagnosis.*—This must first be made in regard to the presence of meningitis and secondly as to the variety. In the early recognition of tuberculous

meningitis, the former of these is likely to give the greater difficulty. In children the symptoms at onset may be much like those of any febrile attack or gastro-intestinal disease. Headache, convulsions, vomiting without cause, respiratory signs, especially sighing respiration, a retracted abdomen, rigidity of the neck, and Kernig's sign are all suggestive.

In children the exanthemata may give difficulty for a few days, but, except in the distinction from typhoid fever, not very long. The appearance of the rash of each disease gives the diagnosis. From typhoid fever, the more irregular fever, the absence of the rose spots, the Widal reaction, the decubitus —dorsal in typhoid fever, lateral in meningitis; the headache, complaint of which, as Sir William Jenner pointed out, ceases in typhoid fever with the onset of delirium, but persists in meningitis, and the results of lumbar puncture, all aid in the recognition of meningitis. Some cases of indefinite, continued fever in children, as, for example, those sometimes seen associated with glandular tuberculosis, may give difficulty for some time. The course and the results of lumbar puncture are the greatest aids. Practically any toxic condition may give difficulty at the onset, such as the toxæmia of any of the infections, or even catarrhal jaundice. In certain instances there has been great difficulty in making a diagnosis from hysteria, beginning mental disease, or delirium tremens. Some intracranial conditions may cause confusion, such as otitis media, thrombosis of the cerebral sinuses, cerebral syphilis, cerebral abscess, and cerebral tumor, especially if tuberculous. It is difficult to lay down rules for the differential diagnosis of these, the absence of the most characteristic signs of meningitis and the results of lumbar puncture being important.

The diagnosis of meningitis being made, the second point, the recognition of the character present, as a rule offers less difficulty. In this all the special features mentioned in connection with the signs and symptoms are important, but by far the greatest aid is lumbar puncture. With care and perseverance, tubercle bacilli may be found in a large percentage of cases. In their absence the finding of a large proportion of mononuclear cells in the fluid must be regarded as suggestive of the tuberculous form. The presence of a definite tuberculous focus elsewhere in the body is of importance. The presence of tubercles in the choroid is positive, but they are not always present. The examination for them should be made every day.

*Prognosis.*—The few recoveries which have been reported, even after the finding of the tubercle bacilli in the spinal fluid or of tubercles in the choroid, stand out as such exceptions, that the outlook must always be regarded as practically hopeless. Recovery has occurred after trephining and drainage.

*Treatment.*—Under prophylaxis it should not be necessary to say that all tuberculous lesions should be treated. We can never tell how many instances of tuberculous meningitis can thus be prevented. When the disease is established, the patient should be kept as quiet as possible, and in a darkened room if there be photophobia. It may not be easy to give food, and if there be difficulty in swallowing, the stomach tube may be necessary. In case of vomiting, various general sedatives may be given and rectal feeding employed. The ice-bag to the head may give relief to headache, but if this be severe, with great restlessness, or convulsions occur, bromide, chloral, or morphine hypodermically should be given. A hot bath, at 105° to 115°, may be given every four or six hours. Blisters and other methods

of counterirritation are to be condemned. They cannot do any good. Lumbar puncture should be repeated at intervals, depending on the amount of fluid obtained, the degree of pressure, and the influence on the symptoms. Surgical methods, such as trephining or opening the spinal canal, have not met with sufficient success to justify their adoption.

II. **Acute Pulmonary Tuberculosis.**—The pulmonary forms of acute tuberculosis can occur in two types, the pneumonic and the bronchopneumonic. Both constitute not more than 10 per cent. of all cases of pulmonary tuberculosis.

1. **Acute Tuberculous Pneumonia.**—This form, known also as acute phthisis, acute pneumonic phthisis, caseous pneumonia, and epithelial pneumonia, occurs more frequently in adults than in children, but is the rarest of the acute forms. It was this form of the disease that led Niemeyer and Virchow to deny the unity of phthisis first advocated by Laennec. Many cases are no doubt instances of confluent multiple foci, but in a few the disease invades a whole lobe at once. Males are more frequently attacked and are often robust and between twenty and forty years of age. The infection is usually bronchogenous, but may be hæmatogenous (Tendeloo). The onset, usually acute, and the course for some days closely resemble those of acute lobar pneumonia. A chill (in 9 of 15 cases, Osler) may usher in the attack and physical signs of consolidation of an entire lobe, usually the upper, develop in a few days. Herpes labialis is not uncommon (Kidd). The bronchial breathing has been described as distant and suppressed, but in many cases this is not so. The sputum is frequently tenacious, rusty and, in fact, for some days closely resembles that of lobar pneumonia. Pneumococci, but no tubercle bacilli, may be present, and unless a previous history of a pulmonary disease can be obtained a diagnosis of frank pneumonia is made. The crisis, however, does not occur, resolution is delayed, the fever assumes a more hectic character, the patient emaciates, and the sputum takes on a greenish tint, first described by Traube. Tubercle bacilli have been found as early as the fourth day (Osler), but more frequently are not discovered until the crisis fails to appear. Elastic tissue is less frequently found than in caseous bronchopneumonia.

When the lower lobe is involved, signs of infiltration may be found at the apex; or if, as is more common, the upper lobe, an infiltration at the opposite apex. The actual physical signs, further, may not agree with the date of appearance of the disease. Dry tuberculous pleurisy is almost always present. The temperature is usually high, but remittent throughout, and from the first shows a wider range than is usual in acute lobar pneumonia, which runs the same course in the tuberculous as in the healthy subject (Fox). The pulse is accelerated and ranges from 100 to 130, while the respirations vary between 30 and 40. Cyanosis is not usually present, but in cases of some duration, anæmia of the lips and mucous membranes is common. The dyspnœa is much less marked than in the acute miliary type. Emaciation is often a prominent feature, and may be accompanied by great prostration. Hæmoptysis sometimes occurs at the onset and may cause death. Albuminuria is infrequent, the diazo reaction rarely absent.

The duration may be but three or four weeks (Tendeloo had a patient die on the sixth day), but more usually it extends over three to four months. A few cases pass into the chronic stage and live for two to five years, but rarely if ever fully recover. The usual course is progressive. Death occurs

chiefly from asthenia, which is frequently aggravated by tuberculous enteritis, laryngitis, and in a few cases from meningitis. Hæmoptysis is not especially frequent and rarely the cause of death.

2. **Acute Tuberculous Bronchopneumonia.**—This form, described under the names of phthisis florida, galloping consumption, or caseous bronchopneumonia, is the more common acute type. In children and the aged it closely simulates simple bronchopneumonia, and the diagnosis may not be made for weeks. Bronchopneumonia in the adult should always be looked upon with suspicion.

The onset is occasionally acute, but more often insidious, with cough. When this acute form supervenes upon a more chronic type, as is common, it frequently follows hæmoptysis and is due to aspiration (Bäumler). It not infrequently follows influenza, or, in children, measles or pertussis. The symptoms are usually pronounced. The cough in some cases, dry at first, soon becomes loose. The sputum, variable in amount, early contains tubercle bacilli and elastic fibers. The patient at first presents a rapid pulse, high, often fluctuating temperature, and quickened respiration. The physical signs, at first indefinite at an apex, soon become more pronounced, and when softening and excavation occur, which are rapid in many cases, chills and night-sweats are common. The patient rapidly emaciates and loses strength. Hæmoptysis is infrequent, but diarrhœa is often present. Death may occur in three or four weeks, but the disease may last three or four months, or the acute symptoms subside and the disease become chronic.

Fränkel recognizes three types of caseous bronchopneumonia. The first, described by Bäumler, occurs in patients already tuberculous, and is due to the aspiration of blood and secretions, often from an old, apical cavity. The resulting symptoms are those of a secondary infection. The second type (due also to aspiration and rarely to hæmatogenous infection) is the peribronchial or nodular. Small, solid, caseous foci, the size of a pea or walnut, are found surrounding a bronchus. Diffusely scattered, fine rales, with little or no dulness, and sputum free from tubercle bacilli, are characteristic phenomena. The third form, the disseminated ulcerative type, frequently following diabetes, pregnancy, alcoholism, influenza, measles, pertussis, usually terminates fatally in two to four months. It is frequent in children between two and six years of age. Rapid loss of weight, anæmia, and hectic fever, with pronounced night-sweats, characterize it. Death from hæmoptysis, meningitis, or general miliary tuberculosis is usual.

III. **Subacute Pulmonary Tuberculosis.**—Comparatively few cases run an acute course from start to finish, but in a very large number the disease is never completely quiescent, but smoulders along with an occasional acute outbreak. The symptoms lessen, the weight and strength increase, the morning temperature falls to normal or below, but each day at some time a temperature of 99.5° to 100° occurs. This may persist for weeks, but sooner or later it gives way to a return of the night-sweats, increased cough and expectoration, with possibly pleuritic pain or dyspnœa; the morning temperature no longer falls as low as normal, and the disease makes rapid headway for a few weeks. This may be repeated for one or two years, but with each successive attack the patient regains his lost strength and weight less readily, the dyspnœa is more continuous, and finally the whole of both lungs becomes involved. Finally, and usually during one of the periods of acute exacer-

bation, the patient dies from asthenia or possibly some slight complication occurs which he is not able to resist. This type is frequent in developing females, follows the puerperium, or occurs when the constitution has been undermined by chronic disease, such as alcoholism, syphilis, or diabetes.

IV. **Chronic Pulmonary Tuberculosis.**—Chronic pulmonary tuberculosis, phthisis, consumption, includes the large majority of all cases of pulmonary tuberculosis. The course, extending usually over about ten years, is marked with many remissions and temporary arrests. Recently some attempt has been made to limit the terms phthisis and consumption to those advanced cases of pulmonary tuberculosis where secondary infection has occurred, an event by no means uncommon. Many chronic cases begin acutely and continue so for some little while. Every acute form may become chronic, even miliary tuberculosis of the lungs. The distinction between acute and chronic forms depends largely upon the fever. In the first it is constant, remittent, intermittent, or even absent for a short but fleeting period. In the second it is absent for long periods and its recurrence is usually marked by an increase of symptoms.

The patient has often been failing almost imperceptibly for several months, when after a slight hæmoptysis, or a little "cold," the temperature rises and cough and expectoration begin. Physical signs, before absent, are now noticed above one clavicle. These are the circumscribed acute cases of Fränkel, which almost without exception run later a chronic course. The patient apparently recovers from the slight acute attack, only to suffer a little later from one more severe. The disease may remain stationary at one place, or even improve, while advancing in another. Two well-defined subdivisions may be made: the ulcerative and the fibroid form.

1. **Chronic Ulcerative Pulmonary Tuberculosis.**—This form, the usual type, is characterized in well-marked cases by cavity formation and induration. The disease has usually long periods of quiescence, or arrest may go on to cure. In other cases at infrequent intervals acute attacks, passing usually as "colds," occur, and in each a slight extension of the disease takes place. The lesions are usually most marked at one apex, where signs of cavity are present. In some cases hæmoptysis is of frequent recurrence, although it may exert but little influence upon the course.

2. **Fibroid Phthisis.**—Some cases of chronic phthisis are characterized by the extensive formation of fibrous tissue. Caseation and ulceration when present are usually overshadowed by the fibroid changes, which, however, may advance to a marked degree without any gross destructive changes. The disease may last from ten to twenty years or even longer. The most marked alterations in the shape of the chest occur in these cases; one apex or base may be greatly retracted, move little or not at all, and present marked dulness. The heart is often displaced, murmurs are common, and in some cases hypertrophy of the right side occurs, with possibly signs of deficient aëration, first noticed in the nails and lips.

Dyspnœa on exertion may be pronounced, and with the sluggish circulation causes the patient to lead, indeed, a "reptile scale of existence." Dilatation of the bronchi is common. The cough is often paroxysmal and apparently, while effective, of little force. Fever may be absent for long periods or very slight when present. Hæmoptysis is not infrequent. The onset is rarely acute. Well-proportioned individuals, Meissen thinks, with a proper relation between height and girth, present the fibrous form much more

frequently than those more poorly built, who approach the habitus phthisicus. Mature age also more frequently presents the fibrous form.

Fibroid disease of the lungs was long looked upon as a pathological entity, but, as West has pointed out, the fibroid changes are usually limited to one lung or a portion of one lung, rarely involve the whole or both, as is common in sclerosis of the liver or kidneys, and rarely occur in other organs. The original tuberculous disease may be entirely replaced by these fibroid changes. Clarke in his monograph distinguished three forms of fibroid phthisis: (1) Tuberculo-fibroid, the generally accepted fibroid phthisis; (2) fibro-tuberculous, the fibroid disease supposed to be primary, the tuberculosis secondary; and (3) pure fibroid, without apparent cause of the fibrosis, a point criticised by West. Patients with fibroid phthisis are threatened with three dangers, as Osler has pointed out: (1) Hæmoptysis, usually profuse; (2) extension or generalization of the tuberculosis; and (3) failure of the hypertrophied heart.

**Latent Pulmonary Tuberculosis.**—This term is used to include forms in which the symptoms or the physical signs may be latent. In the one the symptoms may be suggestive or even pronounced, but physical signs are often lacking on repeated examinations. On the other hand, a routine examination of the chest, often made on an applicant for life insurance, reveals the presence of well-marked physical signs, where little or no history of symptoms can be obtained (masked pulmonary tuberculosis). In either case, more often, however, in the former, the sputum may remain free from tubercle bacilli (closed pulmonary tuberculosis). In this group belong the cases of phthisis ab hæmoptoë, or sudden pneumothorax in apparently healthy patients. Many patients dying of other diseases are found to be tuberculous at postmortem. A primary to say nothing of a pure tuberculosis of the bronchi is clinically unknown, Hoffmann thinks, but he believes it exists. These patients present the complicated symptoms of advanced pulmonary tuberculosis.

A small number of patients present very indefinite pulmonary signs throughout the course. Tubercle bacilli occur in their sputum, and, while some have no doubt a deep-seated pulmonary lesion, in others the affection lies unquestionably in the bronchial glands. Hall thinks hæmoptyses in these patients are usually severe.

Chronic excavation may exist with every appearance of health. The physical signs and symptoms are not determined by the size of the cavity, which may develop slowly, with few symptoms. Cure rarely occurs after the formation of a cavity, but arrest is frequent, and many patients with a limited cavity at one apex enjoy years of comparative health. The cavities in these cases are usually dry and lined with a smooth, glistening membrane. The physical signs gradually disappear from the front, to persist at the apex posteriorly for a long time. In other patients the cavity walls secrete profusely. Some cavities closely simulate pneumothorax; the metallic tinkle, the coin sound, and the displacement of the organs all suggest this complication. Excavation of an entire lobe, unusual and more frequent in men, occurs equally on the two sides, but affects the upper more than the lower lobe. Complete excavation of an entire lung is very rare. Petit believes a cavity may be closed and latent. Fränkel recognized a bronchiectatic form, when the disease, beginning with symptoms of bronchiectasis, exhibits more frequent attacks, severe dyspnœa, and large quantities of sputum.

## COMPLICATIONS.

The complications of so chronic and debilitating a disease are numerous, as we would expect. Some of the intercurrent diseases have little or no effect upon the primary lesion, while others rarely leave it as it was and frequently produce disastrous results. A few seem to be more or less antagonistic. Abrasion of a surface by some intercurrent disease may predispose to a secondary tuberculous infection; or a pleurisy or thoracic deformity may so hinder movement as to render expulsion of the infected matter difficult.

The complications can be divided into those due to the action of the tubercle bacillus or its toxins and those due to other factors. Undoubtedly the complications caused by the tubercle bacillus are always of serious moment, indicating a weakened resistance. Secondary tubercle in primary lung disease may arise in one of three ways. It may be due to direct infection from contact with the sputum, *e. g.*, in the larynx, tonsils, nose, intestines; from direct extension of the disease, *e. g.*, into the pericardium, pleura, chest wall; or the bacillus may be carried, possibly in leukocytes, through the lymphatics or bloodvessels to distant organs. The infection transmitted by this last method may be localized in the brain, meninges, bones, ear, peritoneum or lungs, or be generalized in the peritoneum, serous membranes, lungs, or throughout the body. The toxins in the sputum may produce bronchitis, tracheitis, laryngitis, pharyngitis, and, if swallowed, gastritis, fermentation, and diarrhœa. When absorbed into the circulation they cause in some cases anæmia, neuritis, atrophy, and fatty degeneration of the muscles and even of the heart. In late stages, thrombosis, dropsy, amyloid and other diseases, not peculiar to pulmonary tuberculosis, may occur. No attempt has been made even to mention all the complications.

**Respiratory.—Secondary Infection.**—The chronicity of the disease, the frequency of abnormalities in the upper respiratory tract, especially in the nose, the intercurrent bronchitis, the partial destruction of the ciliated epithelium of the lower air passages, as well as the frequency of microörganisms in the dust of buildings and cities, would all lead us to believe that, the usual defences being broken down, secondary infection is of frequent if not of constant occurrence. But not all cases of pulmonary tuberculosis even at necropsy show secondary organisms in the pulmonary lesion. Ravenel and Irwin have reported three cases of cavity formation which proved to be sterile. Ophüls reported seven out of thirteen. Many tuberculous lungs harbor harmless bacteria, which in no way influence the course of primary disease. These should not be spoken of as instances of mixed infection, but the term should be reserved for those cases in which one or more secondary organisms exert some discoverable influence upon the symptom complex.

While secondary infections are usually looked upon as harmful, some hold that they may exert a favorable influence upon the pulmonary tuberculosis (Sata). Koch in his first publication upon the etiology of tuberculosis called attention to these secondary organisms and their influence upon the symptoms and course. It is probable that the prevailing secondary organism in patients in large cities is not always the same. Many and in fact the majority of the organisms which are almost constantly present in advanced stages have been shown to possess little or no pathogenicity for animals.

The organisms recovered from the lungs are nearly always of low virulence,

and in one instance a streptococcus obtained at autopsy, very virulent for animals, was found on subcutaneous injection into man to produce only local changes, suggesting those of an insect sting. Cornet, who found many of the secondary organisms pathogenic, states that in the same lung in one lesion the complicating organism (streptococcus) may be virulent and in another innocuous. Sata would separate latent from effective mixed infections, and thinks the latter occur in most cases of severe phthisis. Their effect, therefore, upon the patient is still not yet definitely determined, notwithstanding the claims of many competent authorities, who would attribute to the secondary infection the disintegration of the pulmonary tissue (Prudden), the fever, and the streptococcus curve, as well as an abundant expectoration and spreading pneumonia. Cornet and Kossel have found tubercle bacilli and other organisms intimately associated in pathological specimens, particularly in the inner zone of the cavity wall. It is impossible to exclude preagonal and postmortem invasion by the secondary organisms.

Microörganisms have rarely been recovered with unimpeachable technique from the blood in pulmonary tuberculosis unless the patient was *in extremis* (Jochman). This throws considerable doubt upon the occurrence of a condition in pulmonary tuberculosis at all comparable with septicæmia, and suggests that other factors might be the cause of the fever (*e. g.*, the toxins of the tubercle bacillus, of the secondary organisms, or of the disintegrating tissues). Numerous observers have held that the tubercle bacillus and its toxin are alone rarely the cause of fever. Many to-day oppose this view for the following reasons: The injection of tuberculin or of tubercle bacilli in pure cultures causes fever under certain conditions, when secondary organisms can be almost positively excluded. The avirulence of the secondary organisms has been mentioned, as well as their absence in the blood. Fever, Kerschensteiner thinks, gives no information in regard to secondary infection, and he holds joint and cardiac affections, non-tuberculous disease of the serosa, emboli (especially of the retina), or metastatic abscesses as necessary before diagnosing secondary infection.

Careful work has been done to determine if possible the bacterial variation coincident with increase of symptoms. Several observers (notably Hastings and Schroeder and Mennes) have been unable by bacteriological studies to find any difference in the sputum before, after, or during an acute exacerbation, which formerly would have been attributed unquestionably to secondary organisms. Still the grave importance of some mixed infections cannot be questioned. On the whole it seems as if mixed infection was not as important as some would have, but that it is not to be neglected is borne out by the fact that the majority of patients with pulmonary tuberculosis do far better in the country, when removed from constant reinfection with secondary organisms from the dust of cities. The careful isolation of all patients with colds, acute bronchitis, influenza, and tonsillitis, and the exclusion of all visitors suffering from such complaints is another proof of this.

Much light may yet be thrown upon this difficult subject by the study of the patient's opsonic index to the various secondary organisms recovered from the sputum. If after vaccination with an organism to which the patient had a low opsonic index he showed marked signs of improvement, it might be justifiable to call such an infection "mixed" as well as "secondary."

**Upper Air Passages.**—The tendency to contract colds and other affections of the upper respiratory tract is very marked. Moeller and Rappoport in

a recent report have shown that in 120 patients with pulmonary tuberculosis the nose showed some pathological change in 84 per cent., the pharynx in 76 per cent., and the larynx in 42 per cent.

**Tuberculosis of the Nose.**—This uncommon complication usually attacks the cartilaginous septum, but may occur at the juncture of the skin and mucous membrane.

**Pharynx.**—Pharyngeal tuberculosis occurs as a complication usually late in pulmonary tuberculosis.

**Tonsils.**—The tonsils are frequently found at postmortem to be tuberculous, but as the condition gives no definite symptoms nor characteristic appearance it is rarely recognized clinically.

**Larynx.**—This is discussed elsewhere. (Diseases of the Larynx, p. 630.)

**Aphonia.**—This may occur from hysteria, a functional paresis of the adductor muscles of the vocal cords (especially common in women), from pressure of enlarged glands, bronchial or cervical, apical infiltration and shrinking, or pleurisy, upon the recurrent laryngeal and resulting paralysis (rare), and from mucus or secretion on the vocal cords (transitory), as well as from tuberculous involvement of the larynx.

**Trachea.**—This is rarely affected except in far-advanced stages, and is usually associated with laryngeal tuberculosis.

**Bronchi.**—The larger bronchi are not often affected, and then only in late stages, when the ciliated mucous membrane is destroyed. A large percentage of cases of fibrinous bronchitis occur in pulmonary tuberculosis, which has been considered an etiological factor. Bronchitis may be said to be a constant accompaniment of pulmonary tuberculosis, and while in most instances it is due to irritation from the toxins of the sputum and secondary organisms it may be a true tuberculous bronchitis.

**Bronchopneumonia.**—Simple bronchopneumonia occurs in many cases as a complication.

**Lobar Pneumonia.**—Acute lobar pneumonia is, at least in health resorts, rarely diagnosed among the complications of pulmonary tuberculosis. It appears to be of more frequent occurrence in large cities. When it occurs in a tuberculous patient it may run its ordinary course and terminate either by lysis or more rarely by crisis. Fowler and others, however, oppose this view, and think it a grave but rare and aggravating complication in chronic pulmonary tuberculosis.

Recent work of Flick, Ravenel, and Irwin has given the pneumococcus an added interest in its probable connection in some instances with hæmoptysis. It must not be overlooked that A. Fränkel has found the pneumococcus along with the tubercle bacillus in caseous pneumonia.

**Gangrene and Abscess.**—Gangrene of the lung rarely occurs in pulmonary tuberculosis (in less than 1 per cent., West). In a few instances the walls of a cavity become gangrenous, but this is much more unusual than the fœtid decomposition of the secretions in cavities. Abscess also seldom occurs.

**Bronchiectasis.**—This, while rare in the more acute forms, is far from unusual in fibroid phthisis.

**Emphysema.**—This is frequent in pulmonary tuberculosis and in some instances may mask it. Compensatory emphysema, however, is frequently found in chronic cases on the less affected side, and may be so marked that the lung extends well across the middle line.

Interlobar emphysema may occur. In rare instances caseation of a bronchial gland may lead to ulceration of a bronchus, or the rupture of an adherent cavity into the tissues of the chest wall may occur, which produces general subcutaneous emphysema. Death quickly results.

**Atelectasis.**—Areas of atelectasis are frequent in patients, usually middle aged, in advanced stages, with shrunken chests.

**Asthma.**—Pulmonary tuberculosis rarely occurs in an asthmatic, but asthmatic attacks are not infrequent when the tuberculous disease becomes chronic and the fibrosis pronounced.

**Pleura.**—Pleurisy occurring in tuberculosis has been grouped by Osler under three heads: (1) Acute tuberculous pleurisy, (2) subacute and chronic pleurisy, and (3) general serous membrane tuberculosis.

*Dry pleurisy* may be said to occur almost constantly in pulmonary tuberculosis from extension of the process to the pleura. It may be primary (miliary tubercle). The work of Hodenpyl leaves little doubt that the majority of obliterative pleurisies are tuberculous. Marked thickening of the pleura may occur, but this condition usually follows an effusion. In acute, dry pleurisy effusion should be suspected when pain suddenly ceases.

*Pleurisy with effusion* is far from infrequent in pulmonary tuberculosis, although it occurs much more frequently at its onset than during its course. The effusion is usually (80 per cent.) serofibrinous, but may be serous or in rare instances hemorrhagic, which betokens an unfavorable and usually rapidly fatal course (Moutard-Martin). In some acute as well as in chronic cases the fluid is slightly greenish or opalescent. Chyloform or milky exudates may occur.

**Pneumothorax.**—Pulmonary tuberculosis is said to be the cause of 80 to 90 per cent. of all cases of pneumothorax. It is, however, a rare accident in the incipient stage, and postmortem figures, including a number of undiagnosed cases, show it to occur in about 5 per cent. of all autopsies in pulmonary tuberculosis. The higher percentages of Williams (10 per cent.) and of Dittrich (14 per cent.) may be explained by the fact that many uncomplicated cases were not autopsied, though Stanton reports 9 per cent. in 111 autopsies. The lung must be at least partly free from adhesions, and usually a rapidly advancing caseous process with cavity formation is found just under the pleura, at the point of rupture. Pneumothorax occurs in the acute pneumonic or caseous type of pulmonary tuberculosis, which, however, may supervene upon a more chronic process. It never occurs in the fibroid form, and no cases have been reported in acute miliary tuberculosis of the lungs.

The subphrenic abscess described by Leyden may closely simulate pneumothorax, and in some instances cavity may present every physical sign, although the heart and liver are usually drawn toward the affected side.

The results of pneumothorax may be divided into immediate and remote. They depend, especially at first, upon the general condition and more particularly upon the condition of the opposite lung. When the result is not immediately fatal, effusion almost always takes place. The effusion was serofibrinous in all of Spengler's patients who recovered, but he believes that recovery can take place even in pyopneumothorax. The effect in the compressed lung has been held to be favorable. On the other hand, the opposite functioning lung is often observed to become more involved. On the whole, it may be said that pneumothorax is always a serious complication, and with rare exceptions, results in death.

**Empyema.**—This is seldom met with in pulmonary tuberculosis, and then usually in advanced stages and following pneumothorax, but it is always a serious complication.

**Eye.**—Tuberculosis of the eye or its appendages is rare in pulmonary tuberculosis.

**Ear.**—The close connection between the nose and the ear and the frequency with which changes occur in the former lead us to believe that the ear in patients with pulmonary tuberculosis is frequently affected, although possibly not so often as Moeller and Rappoport found (76 per cent.).

Tuberculosis of the middle ear, more common in males, is rather frequent.

**Gastro-intestinal.**—Complications occur more frequently in the gastro-intestinal than in any other system. Thrush may penetrate into the glands, and form thrombi and metastatic brain abscess. Stomatitis is infrequent in patients with good surroundings, but may be severe and last two weeks. Aphthous ulcers are common. Pyorrhœa alveolaris is not inlrequently seen, and slight gingivitis is not uncommon. Dental caries is frequent and of great importance on account of imperfect mastication, and of infection with tubercle bacilli or secondary organisms. Alveolar abscess is rather frequent.

Tuberculosis of the buccal cavity is of very rare occurrence; the tongue and the tonsils are most often attacked. The tongue, from frequent slight injuries, is rendered more liable to infection, which usually occurs upon its tip or edges. The gums and hard palate are attached more rarely than the soft palate, uvula, and pillars of the fauces. The posterior pharyngeal wall and the lips are rarely affected. Tuberculosis of the salivary or parotid glands is uncommon.

**Œsophagus.**—Complications in the œsophagus are very rare. Tuberculous disease of the gullet occurs only when the lumen has been narrowed by stricture (circular ulcer, possibly carcinomatous) or dilated and diverticula formed (W. Fox).

**Gastric Tuberculosis.**—Tuberculosis of the stomach, while never primary, is a very rare complication of pulmonary tuberculosis. Various explanations have been offered of its rarity, and Blumer in an excellent *resumé* of the subject concludes that the acidity of the gastric juice in healthy conditions is probably sufficient to prevent the development of tuberculosis, but insufficient if a local point of lessened resistance occurs. Males are more often affected than females. The most frequent site is the pylorus, and the ulcers were multiple in one-half of the cases collected by Blumer. Miliary tuberculosis of the stomach occurs in general miliary tuberculosis. The ulceration often produces remarkably few symptoms, and may be entirely overlooked.

**Gastric Ulcer.**—Simple ulceration occasionally occurs in pulmonary tuberculosis, although De Renzi thinks it very common (22 per cent.); 2 instances have occurred in 1000 cases at the Adirondack Cottage Sanitarium.

**Intestinal Tuberculosis.**—This is the most frequent of all tuberculous complications in chronic pulmonary tuberculosis, but is rare in the acute forms. It is common only in the more advanced stages, and the great discrepancy which exists between the symptoms in life and the postmortem findings can be explained only by its latency.

The symptoms are notoriously uncertain. Diarrhœa may be absent throughout or alternate with constipation. The diarrhœa depends less upon the extent of the ulceration than upon its site (more pronounced if in the lower colon) and upon the accompanying catarrhal inflammation.

The stools vary greatly in frequency and physical characteristics. Blood

in any quantity is rare, but several instances of death from intestinal hemorrhage have been reported. The discovery of tubercle bacilli in the stools is of little value, for in a large proportion of all patients with pulmonary tuberculosis they are present if the sputum contain tubercle bacilli.

Nausea may be present and thirst is often marked. Pain, more often low in the abdomen, is usually colicky and occurs with greatest intensity after food or before defecation. It may be slight or severe and continuous. Chronic diarrhœa in pulmonary tuberculosis is most often associated with intestinal tuberculosis. The most important complications are perforation and stenosis. Tuberculous stenosis of the intestines may occur from concentric hypertrophy in the hypertrophic form or from contraction of scar tissue, formed in a cicatrizing ulcer. The *hypertrophic form* of intestinal tuberculosis occurs chiefly about the ileocæcum. The connective-tissue hypertrophy causes a concentric narrowing, although tumors are found at times closely resembling malignant growths. Middle-aged males with slight or slowly advancing pulmonary disease are usually attacked.

**Appendicitis.**—Simple appendicitis cannot be said to occur more frequently in patients with pulmonary tuberculosis than in the healthy. It runs its usual course and the same indications for operation exist. Tuberculous appendicitis was formerly considered rare, but has recently been found to be of more frequent occurrence. The symptoms are often so slight and so obscured by the preëxisting pulmonary and intestinal tuberculosis that the appendicular disease is first discovered at necropsy.

**Rectal Ulceration.**—This is fortunately not common, as it can cause severe pain, both continuous and increased on defecation. If attempts at healing occur, stenosis may result, which, however, is rare, as the condition is usually found only in advanced stages of pulmonary tuberculosis.

**Fistula-in-ano.**—*Ischiorectal Abscess.*—Fistula is a rather frequent complication, occurring in about 3 per cent. of all cases. It rarely occurs in early life, is uncommon before twenty, most frequent from twenty to forty, and is by no means rare in senile tuberculosis. It may first call attention to the pulmonary disease, or it may, as is more usual, occur in advanced stages associated with ulceration of the rectum. The onset is usually with a perineal or ischiorectal abscess, which (when incised) fails to heal. The chief symptoms are: severe pain, especially on coughing and on defecation, but after free drainage is established the symptoms may be so slight as to escape the patient's notice. Many of such fistulæ have no opening into the rectum. In early cases a fistula may exist and cause little or no trouble, and in some cases may precede the pulmonary symptoms by years.

**Peritonitis.**—Acute peritonitis rarely complicates pulmonary tuberculosis, and, when it does occur, follows most often acute appendicitis or perforation of a tuberculous ulcer. Peritoneal tuberculosis is infrequent in pulmonary tuberculosis, and most often consecutive to some abdominal complication, *e. g.*, tuberculosis of the mesenteric glands, of the intestine. or of the Fallopian tubes.

**Liver.**—Complications of the liver have more pathological than clinical importance. Tuberculous lesions are rarely diagnosed, although very frequent at autopsy.

**Circulatory System.—Heart.**—The coincidence of pulmonary tuberculosis and heart disease, formerly regarded as rare, is now known to occur in about 1 per cent. of all cases of pulmonary tuberculosis. The apparent antagonism between the two was attributed by Walsh to the different age incidence,

by Graham to the increased amount of blood in the lungs, especially in the bases, causing increased expansion of the apices. In 69,659 cases of pulmonary tuberculosis collected from all sources, valvular disease of the heart occurred in 747 (1 per cent.). In 77 of these, the mitral was involved in 68 (insufficiency 44, stenosis 13, insufficiency and stenosis 3, unclassified 8); the aortic in 7 (stenosis 2, insufficiency 1, unstated 4); the mitral and aortic in 1, the pulmonary in 1 (stenosis). Meisenberg found, among all patients at the Leipsic clinic from 1889 to 1898, that 13 per cent. had pulmonary tuberculosis and 1.75 per cent. had heart disease. Of the latter 7 per cent. had pulmonary tuberculosis; of the former, 1.14 per cent. had heart disease. This would seem to indicate that given either disease the other is less likely to occur. In 8154 autopsies upon patients dead of pulmonary tuberculosis, cardiac disease was found in 293 (3.5 per cent.), and in 388 autopsies upon valvular heart disease, pulmonary tuberculosis was present in 26 (6.6 per cent., Norris). Pulmonary stenosis may always be said to be the primary disease, but mitral stenosis rarely if ever.

Acute endocarditis occurs in 5 per cent. of the cases of pulmonary tuberculosis. Tuberculous endocarditis is exceedingly rare.

Mitral insufficiency is the type most frequently found in pulmonary tuberculosis, as the age incidence is more nearly similar. It is said not to predispose to pulmonary tuberculosis, and, if the compensation be good, may exert no unfavorable influence upon the pulmonary disease, and may even retard it. Mitral stenosis was held with some reason by Traube and Lebert to be distinctly inhibitory to pulmonary tuberculosis, which is usually of an abortive form. The prognosis is good. Aortic insufficiency occurred in 5.4 per cent. of Meisenburg's Leipsic cases. It is much less apt to be found with active than with healed pulmonary tuberculosis, as v. Kryger's experience would show. Pulmonary stenosis, always congenital, is commonly agreed to predispose to pulmonary tuberculosis, which, however, may develop slowly, although it is frequently miliary (Fox).

Jaccoud has observed many instances of tricuspid insufficiency with venous pulse, but in the experience of others it is rare. Tricuspid insufficiency may be a great source of danger in benign chronic cases with sclerosis.

Pulmonary tuberculosis may be said to occur, therefore, most frequently in pulmonary stenosis, least often in mitral stenosis, and more commonly in mitral insufficiency than in disease of the aortic valve. West, however, believes mitral disease is least frequently found with pulmonary tuberculosis. The prognosis and treatment depend upon the prognosis and treatment of the predominant disease. The patients usually do well on account of the hypertrophy until the compensation is broken, and then the pulmonary tuberculosis may quickly advance (Abram).

Hypertrophy or dilatation of the right ventricle, especially in patients with pleural thickening and shrinking, is not infrequent (Bohland). It is difficult to detect by percussion, but the orthodiagraph often shows it clearly. It is evidenced, also, by epigastric pulsation and accentuation of the second pulmonic sound. The reserve force, however, of such a heart is slight, and dyspnœa and a rapid pulse quickly follow forced exertion.

**Pericarditis.**—Tuberculous pericarditis is not common in pulmonary tuberculosis. In 1780 autopsies of tuberculous subjects it occurred 81 times (4.6 per cent., Norris). It is usually secondary, and is often overlooked. It may arise from direct extension from the pleura or from perforation from a tuberculous cavity. It occurs in children more frequently than in adults

and in men more than in women. The course tends to be chronic. Non-tuberculous *myocardial* degeneration is not rare. Brown atrophy and fatty degeneration are the most frequent forms of all cardiac complications. Myocardial tuberculosis is very infrequent and is often secondary to tuberculous pericarditis.

**Arteries and Veins.**—Arterial and endocardial thickening is not a common result, possibly on account of the age distribution, occurring in 2.43 per cent. of 2344 patients at the Phipps Institute, Philadelphia. Embolism rarely occurs and is recognized in the lungs only when a hemorrhagic infarct forms. Thrombosis is not uncommon, occurs more frequently in the veins, and usually when cachexia is marked. Aneurism of the aorta occurs infrequently.

**Anæmia.**—Pernicious anæmia and leukæmia rarely coexist with pulmonary tuberculosis. In the former the blood picture may improve as the tuberculosis grows worse (Ehrlich), and pulmonary tuberculosis occurring as a complication of leukæmia may essentially modify the blood findings.

**Chlorosis.**—Chlorosis and pulmonary tuberculosis are so frequently found in the same patient that many declare that chlorosis is but an early symptom of tuberculosis (Landouzy, Labbe).

**Nervous System.—Mental Diseases.**—While many pulmonary patients develop marked nervous symptoms, mental derangement rarely occurs. In mental diseases, on the contrary, pulmonary tuberculosis is of frequent occurrence.

**Meningitis.**—Tuberculous meningitis, always a terminal complication, occurs in about 8 per cent. of all cases. All the symptoms of meningitis can occur and at postmortem no gross lesions be observed. Spinal meningitis can occur alone as well as cerebral (basilar), but is rare and almost always exists in the cerebrospinal form as meningomyelitis.

A tuberculous infiltration of the brain or cord occurs, and instances of solitary tubercle complicating pulmonary tuberculosis have been reported. The cerebellum and cerebral hemispheres are most often attacked. The lesion may not cause symptoms, or signs of brain tumor may be present. Young male adults are usually attacked. Solitary tubercles in the cord may cause no signs or produce paralysis.

**Genitals.**—Tuberculosis of the genitals is not common in pulmonary tuberculosis, but when it occurs is most frequent in the testicles and Fallopian tubes. Tubal disease may cause prolonged intermittent fever, with slight symptoms referable to the genitals. Tuberculous ulceration may occur in the vulva or uterus. Chronic non-tuberculous inflammatory conditions or tumors of the pelvic organs may exert a marked deleterious effect upon the pulmonary disease.

**Urinary Organs.**—Secondary tuberculosis in the genito-urinary system, apart from the kidneys, rarely occurs in pulmonary tuberculosis (Krzywicky places it at 5 per cent.). In Fowler's postmortem statistics of 531 cases of pulmonary tuberculosis, tuberculosis occurred in the bladder in 4 cases, in the suprarenals in 4, in the epididymis in 9, in the prostate and seminal vesicles in 6, in the tubes and ovaries in 9. Clinically, these conditions manifest themselves much more rarely.

**Nephritis.**—The frequency of nephritis varies much with different observers. Some (Delafield and Prudden, De Renzi) hold that at autopsy it is rare to find the kidneys microscopically intact, but if this be so a large proportion of the cases must remain latent. Recent careful clinical observa-

tion, however, has revealed much more frequent changes than were formerly suspected. In slowly progressing forms interstitial nephritis is the most frequent, and in the subacute type the parenchymatous (Plicque); but the latter form is said to be much more common. Amyloid disease is much less frequent. Recently a number of observers have described a series of cases of bacillary nephritis without tubercle formation or caseation, which tend to undergo fibrosis.

The nephritis may affect the symptoms of the primary disease to a certain extent. The temperature may become lower, the pulse faster, and the blood pressure higher. The specific gravity of the urine is high and a few hyaline and granular casts are nearly always present. The symptoms, however, may disappear for several months. Albuminuria is not always present even when extensive lesions exist in the kidneys. Renal complications are usually insidious in their onset and slow in their course. Cardiac hypertrophy is unusual.

Tuberculosis of the kidneys occurred in 6.5 per cent. of 531 necropsies in pulmonary tuberculosis (Fowler and Godlee), while Harris and Beale found it in 9 per cent. of 200, and Bamberger in 15 per cent.

Uræmia is rare in patients with much œdema, and usually develops slowly. The dyspnœa of uræmia is no doubt often overlooked. It may simulate asthma, appear suddenly and at night. In some cases Cheyne-Stokes breathing occurs. Convulsions are rare, and whether the delirium is due to this condition is hard to say.

In a study of the kidneys based upon 59 cases of pulmonary tuberculosis, which came to autopsy at the Phipps Institute and upon one autopsy of healed pulmonary tuberculosis, Walsh found tubercles in 58 per cent. Besides these there were 3 cases of "probable tubercles" and 5 of definitely healed tubercles, making in all 43 instances. Many of these were only diagnosed microscopically. In 14 out of 17 cases the urine contained tubercle bacilli, found by experimental inoculation. Œdema and albumin were the rule. The discovery of casts and pus cells depends on the carefulness of the observer, ranging from 13 to 40 per cent. The heart was usually normal, and, when abnormal, was nowise associated with the kidney condition. The most common clinical manifestation of nephritis in tuberculosis are hyaline and granular casts, tubercle bacilli in the urine, and less frequently pain or aching in the lumbar region, albumin in the urine, œdema and looseness of the bowels, which may alternate with constipation, as well as unusual fatigue upon slight exertion, unaccountable dyspnœa, and rapid pulse (Walsh).

**Albuminuria.**—This is rare in incipient pulmonary tuberculosis. It was present at some time after repeated examinations in 62 (5 per cent.) of 1214 patients in all stages at the Adirondack Cottage Sanitarium and is not always present in tuberculous nephritis. It is usually due to a renal lesion, but may be caused, Le Noir holds, by hyperthermia, by disturbance of the alimentary tract or of nutrition of the liver, and by cachexia. Always of unfavorable prognostic significance, it demands cessation of treatment of the pulmonary tuberculosis only when pronounced. Albumoses are said to have been found in the urine of patients who after vigorous exercise suffer from fever (Ott). Their presence has been suggested as a contra-indication for exercise, but is of little value.

**Pulmonary Tuberculosis in Nephritis.**—Pulmonary tuberculosis occurs in nephritis as frequently as nephritis is found clinically in pulmonary tuberculosis. Secondary tuberculosis may run a slow course in chronic nephritis

and the fibroid type is common. In amyloid disease of the kidney 37 per cent. are said to have had pulmonary tuberculosis. Senator finds that in Berlin chronic parenchymatous nephritis is due more frequently to tuberculosis than to any other chronic disease.

**Cutaneous System.**—The skin frequently presents changes, which, however are rarely of a tuberculous nature. Chilblains occur frequently and the tendency to a vascular paresis present in many cases no doubt favors the development of erythema pernio. Pernin has shown that over two-thirds of his phthisical patients had chilblains, while of the healthy servants at the sanatorium less than 15 per cent. had them. He believes that this erythema is due directly to the tuberculous toxin.

Purpura hemorrhagica rarely occurs, but a fatal case has been reported. Its occurrence may coincide with a marked change for the worse or a generalization of the disease. But 3 well-marked cases of purpura have occurred in the last 1000 cases at the Adirondack Cottage Sanitarium. One was a typical case of Henoch's purpura in a man of thirty-one; another was associated with joint symptoms. Herpes zoster is not uncommon.

Tinea or pityriasis versicolor occurs in about 5 per cent. of favorable cases. Various forms of erythema have been described. A macular form is more common in acute tuberculosis and the other forms are rare. Lupus occurs very rarely as a complication of pulmonary tuberculosis, in 6 (0.08 per cent.) of 7485 sanatorium patients collected by Sallis; tuberculous warts (verruca necrogenica) are of extreme rarity.

**Lymphatic Glands.**—In chronic pulmonary tuberculosis old cicatrices in the neck are not rare. Enlargement of the cervical and axillary glands does take place in a few cases, and in some the glands break down and suppurate, although usually they are just palpable and remain unchanged. In some instances the pus may be loaded with tubercle bacilli. Enlarged tracheal or bronchial glands may cause symptoms referable to compression. The physical signs of enlarged bronchial glands, usually more evident in children, are rarely well marked in adults. The symptoms may all subside, or suppuration or resolution occur. The *salivary glands* are rarely affected, although stoppage of Wharton's duct may lead to alarming degree of swelling.

**Thyroid Gland.**—This is frequently slightly enlarged. Stanton has recently called attention to the comparatively frequent occurrence in pulmonary tuberculosis of symptoms similar to those met with in disease of the thyroid gland, where there is apparently increased activity, and to the frequency with which tubercles are found in this gland at autopsy. Turban found slight hypertrophy of this gland in 20 per cent. of his pulmonary patients, usually associated with tachycardia.

**Mammary Glands.**—Hypertrophy may occur, but is unusual, and is more frequent in men.

**Superficial Thoracic Abscess.**—Superficial cold (tuberculous) abscess of the thorax is not common in pulmonary tuberculosis. It is usually connected with tuberculous osteitis of the ribs or sternum, or arises from the pleura or lung, but in some instances lies deep under the pectorals and seems to be primary in the muscle. At times these abscesses closely simulate a pointing empyema. In rare instances a cavity may ulcerate through the chest wall and be mistaken for empyema.

**Amyloid Disease.**—This is now infrequent as a complication of pulmonary tuberculosis. Zahn in 2058 cases of tuberculosis found amyloid disease in less than 5 per cent. When it occurs it usually affects several organs

simultaneously, particularly the spleen, kidneys, intestines, liver, and stomach. Amyloid disease is said rarely to curtail life.

**Diabetes Mellitus.**—This is frequently complicated by pulmonary tuberculosis, which runs a fatal and usually acute course. It is exceedingly rare for diabetes mellitus to occur in pulmonary tuberculosis. Hæmoptysis is rare; the sputum may contain sugar, the sweats are less abundant and the temperature less elevated in pulmonary tuberculosis when associated with diabetes mellitus. Diabetes insipidus occurs very rarely in tuberculosis.

**Carcinoma.**—Cancer and tuberculosis were long looked upon as antagonistic (Rokitansky), but it has been shown that the age incidence and the localization of the two diseases are so different that any apparent antagonism is easily explained (Mock). More recently, Rokitansky's experiments, published by Baumgarten, have shown that bovine tubercle bacilli failed when inoculated to infect six patients suffering from inoperable cancer. The results were controlled by autopsy. Schwalbe has reported three cases of cancer developing in the wall of a tuberculous cavity, and Claude thinks that tuberculosis is not uncommon in cancerous deposits. A study of Riffel's monograph upholds the view that pulmonary tuberculosis is not more common in individuals with cancerous antecedents.

**Syphilis.**—Considering the frequency of both diseases their coexistence is uncommon. The lues is more frequently contracted first, and no doubt often plays an important part etiologically in regard to the pulmonary tuberculosis. Otis' figures, which seem to show that a large proportion of dispensary patients with syphilis, and with no discoverable sign of tuberculosis, react to tuberculin, lend interest to this disease in regard to diagnosis. The frequency of tuberculosis in syphilitic lungs is borne out by Hansemann's figures, who found tubercle bacilli in 17 out of 22 cases.

**Vaccination.**—The revaccination of patients with pulmonary tuberculosis demands careful consideration. Five years ago (1902) it became necessary to revaccinate 42 of the patients at the Adirondack Cottage Sanitarium and in the surrounding region. It was effective in 24, and of these 6 were affected more or less severely and were not so well for some time. It is therefore well to avoid vaccination if possible in the advanced stages, and safer in all cases where practicable to isolate the pulmonary patients. In the incipient stage little effect was noticed.

**Diphtheria.**—The age incidence of diphtheria and the comparative rarity of the exposure of consumptives to the disease no doubt account for their infrequent coexistence. Pulmonary tuberculosis does not seem to influence the diphtheria, and 7 patients with combined diphtheria and pulmonary tuberculosis at the Adirondack Cottage Sanitarium all showed marked improvement in their pulmonary condition after recovering from diphtheria. The patients should be kept in bed out-of-doors, and antitoxin used as in ordinary cases. In an institution prophlyactic doses of 500 units should be repeated every two weeks as long as necessary. Caution is necessary when the pulmonary tuberculosis is complicated by enlarged lymph nodes.

**Rheumatic Fever, etc.**—Notwithstanding the rigorous treatment in cold climates, patients with pulmonary tuberculosis rarely have rheumatic fever. Indefinite pains in the joints are common, myalgia not infrequent, but swollen, painful joints are rare. West thinks a real antagonism exists between the two diseases. The writer has seen but 1 instance in 2000 cases. Gout is rarely seen in connection with pulmonary tuberculosis, and some antagonism is said also to exist between gout and pulmonary tuberculosis.

The age incidence is also different. Pollock mentions 7 cases; 2 were over forty years of age and 5 between forty and fifty. Furthermore, as H. Strauss has pointed out, the gouty are well nourished and have a vigorous constitution, two factors which render them less susceptible to tuberculosis. Poncet has recently called attention to a tuberculous arthritis which occurs in tuberculous patients and often results in ankylosis. It is most frequent in children between seven and twelve years of age. It is distinguished from true acute articular rheumatism by its mode of onset, by the slight general and predominant local symptoms (persisting in the joint affected), by the inefficacy of the salicylates, and by infrequency of cardiac complications. Arthritis deformans of the spine may occur in connection with pulmonary tuberculosis, and suggest tuberculous spondylitis.

**Addison's Disease.**—This is a rare complication and only 2 patients out of 2600 at the Adirondack Cottage Sanitarium are known to have had the disease. When associated with pulmonary tuberculosis, Addison's disease is usually fatal. West mentions 7 cases, 2 with chronic pulmonary tuberculosis, and 1 with chronic pleurisy. Pigmentation of the skin may occur in pulmonary tuberculosis with intact suprarenals.

**Pregnancy and Parturition.**—Pregnancy often occurs in pulmonary tuberculosis. Bacon has recently pointed out that pulmonary tuberculosis is at least as frequent in pregnant women as in the general population. From 1 to 1.5 per cent. (about 30,000 in the United States) of all pregnant women may be said to have a discoverable tuberculous lesion (Bacon), and West states that pulmonary tuberculosis is more prevalent among married than unmarried women.

The effects of pregnancy and parturition upon pulmonary tuberculosis are to be separated. Pregnancy, if it causes no nausea or vomiting, often seems to exert little if any influence upon the pulmonary disease. In a few cases the disease is apparently arrested and the nutrition and general and local condition of the patient is much improved during the pregnancy. In acute progressive cases pressure of the enlarged uterus may cause discomfort and dyspnœa; the cough and fever may produce abortion, which, however, occurs less frequently than in heart and kidney disease. Bernheim found that 23 per cent. of 315 pregnancies in tuberculosis were interrupted. The later it occurs in the pregnancy the more apt is abortion to occur. Conception can occur at almost any stage of pulmonary tuberculosis.

The effects of parturition, although it last but five or six hours, are always to be regarded seriously. The prolonged muscular exertion, the loss of blood, the attendant exhaustion, the inhalation of infectious material during the pains, are always serious. The apparent indifference of many physicians to these facts is astonishing.

Pregnancy (including labor) may awaken old, quiescent lesions, and incite fresh ones to renewed activity. Schauta thinks hæmoptysis occurs in 50 per cent. of the cases, a percentage probably much too high. In advanced cases pregnancy is always serious, and, when laryngeal lesions are present, the mortality is said to be 61 per cent. (Fellner). Multiple pregnancies even in cured patients are dangerous. Dubois, quoted and upheld by Osler, says: "If a woman threatened with phthisis marries, she may bear one accouchement well, a second with difficulty, and a third never." The pregnancy frequently runs an uncomplicated course. It is well recognized that after labor or abortion the pulmonary tuberculosis may run a rapid course. This is more often so if tuberculous laryngitis is present.

# CHAPTER X.

## THE DIAGNOSIS AND PROGNOSIS OF TUBERCULOSIS.

By LAWRASON BROWN, M.D.

### DIAGNOSIS.

In no disease is diagnosis more important, for it has been shown by sanatorium statistics that not only the immediate, but the permanent results of treatment are closely connected with and dependent upon the stage of the disease in which the diagnosis is made. Every effort should therefore be made to arrive at a diagnosis as early as possible. He who always waits for tubercle bacilli to appear in the sputum before making a positive diagnosis is apt to come to the conclusion that many cases of pulmonary tuberculosis have slight chances of recovery. Personal acquaintance with a patient or his family should have no negative value in diagnosis.

**Source of Infection.**—The discovery of a source of possible infection is an important point and should always be carefully investigated. This is the most important information to be gleaned from the family history, and a mere enumeration of the deaths occurring in the family from pulmonary tuberculosis, without exact details of the associations between the afflicted members and the patient, is of small value. The habitation, workshop or office, and particularly the fellow-lodgers or employees, should be recalled by the patient to trace a likely source of infection. This is, if present, valuable in diagnosis, but its absence is of no great importance.

**Predisposing Factors.**—Due regard should be paid to the occupation. Those who work in brass, flint-polishers, file-cutters, potters, gold-miners (in quartz), those who are suddenly exposed to extremes of temperature, or to inhalation of irritating vapors, are more susceptible to pulmonary tuberculosis. Great mental anxiety, grief, worry, care, frequent parturition and prolonged lactation, abuse of stimulants, excess in venery, insufficient food, exposure to cold, unsanitary surroundings, and such diseases as measles, whooping-cough, and smallpox, are all of importance. A history of previous adenitis or joint disease is of much value.

**Symptoms.**—In many instances these play a very important part in diagnosis and appear almost invariably before physical signs are manifest in the lungs. Many patients lose their chances of recovery by the dilatory practices of some physicians. Suspicious symptoms should put us on our guard, and after due consideration, if explained fully in no other way, steps to be mentioned later should be taken at once to settle definitely the diagnosis. The localizing symptoms, such as hæmoptysis, cough, and pleurisy, have greater diagnostic value than general symptoms, such as rapid pulse, fever, loss of weight and strength. When two or more are combined it is suggestive of tuberculosis, and if associated with hæmoptysis it is sufficient to subject a patient to treatment. Any of these symptoms following measles or whooping-cough are always of grave import. Persistent, obstinate hoarseness or the history or presence of ischiorectal abscess or fistula always suggests a careful pulmonary examination, even

if only slight symptoms are present. Preëxisting tuberculous lesions indicate a similar course. A combination of loss of weight and strength, fatigue after slight exertion, and loss of appetite, are usually embraced in the term "run down," and together with a slight cough form one of the commonest onsets. Stiffness and pain in the joints is sometimes present early. Oppression under the sternum, sometimes quite marked, and indefinite pains in the chest, especially between the scapulæ, are far from rare. The menstruation may be early affected, and later may entirely cease.

**Fever.**—The bodily temperature plays an important part in diagnosis. Exercise readily causes a rise of temperature (Penzoldt's reaction) in tuberculous patients, and can be made use of when diagnosis is doubtful. The patient may be kept quiet for three or four days, then allowed exercise. A comparison of the temperatures during the two periods may aid greatly in the diagnosis, but other debilitating diseases may act in a similar manner (Burton-Fanning). In healthy women the temperature of the premenstrual period not infrequently reaches 99.5° or higher. In some nervous or fat individuals, as well as during convalescence from infectious fevers, the temperature may be very easily elevated.

A persistent, slight elevation of temperature without apparent cause is a very suspicious symptom, and should always be fully investigated. In a number of cases a persistent afternoon temperature of 99.5° to 100° is the earliest symptom. Williams has called attention to the fact that the temperature is one of extremes, and mentions a case of Lebert's in which 89° was recorded. A subnormal temperature after noon is rare. Disturbed sleep and a slight tendency to sweat may be the only signs of fever.

**Loss of Weight.**—This occurs in the majority of all patients. It is a striking fact that at the Adirondack Cottage Sanitarium the average weight of the patients on discharge, after an average gain of about 14 pounds, and while considerably above their weight in health, is no more than it should be normally. In other words, the consumptive is a person whose weight in health is considerably below the normal for his height and age. No formula expressing the relation between the height and weight has yet been worked out, and all so far advanced are easily proved fallacious. The following table based upon the weights of 77,188 persons in health gives approximately the average weight in health.

Table showing average weight for height and age, based on tables constructed by Oscar H. Rogers, M.D., from the recorded heights and weights of 74,162 insured males and 3016 females. The heights were taken in shoes and the weights with ordinary clothes without coat, or without coat and vest.

MALE.

| Age | 5 ft. | 5 ft. 1 in. | 5 ft. 2 in. | 5 ft. 3 in. | 5 ft. 4 in. | 5 ft. 5 in. | 5 ft. 6 in. | 5 ft. 7 in. | 5 ft. 8 in. | 5 ft. 9 in. | 5 ft. 10 in. | 5 ft. 11 in. | 6 ft. |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 20 | 114 | 117 | 121 | 125 | 128 | 132 | 136 | 140 | 144 | 149 | 153 | 158 | 163 |
| 22 | 116 | 119 | 123 | 126 | 130 | 134 | 138 | 142 | 146 | 151 | 155 | 160 | 165 |
| 24 | 117 | 120 | 124 | 128 | 131 | 136 | 139 | 144 | 148 | 153 | 157 | 162 | 167 |
| 26 | 118 | 122 | 126 | 129 | 133 | 137 | 141 | 145 | 150 | 154 | 159 | 164 | 169 |
| 28 | 120 | 123 | 127 | 130 | 134 | 138 | 142 | 147 | 151 | 156 | 161 | 166 | 170 |
| 30 | 121 | 124 | 128 | 132 | 136 | 140 | 144 | 148 | 152 | 157 | 162 | 167 | 172 |
| 32 | 122 | 125 | 129 | 133 | 137 | 141 | 145 | 150 | 154 | 159 | 164 | 169 | 173 |
| 34 | 123 | 126 | 130 | 134 | 138 | 142 | 147 | 151 | 155 | 160 | 165 | 170 | 175 |
| 36 | 124 | 127 | 131 | 135 | 139 | 143 | 148 | 152 | 156 | 161 | 166 | 172 | 176 |
| 38 | 124 | 128 | 132 | 136 | 140 | 144 | 149 | 153 | 158 | 162 | 167 | 173 | 177 |
| 40 | 125 | 129 | 133 | 136 | 141 | 145 | 149 | 154 | 158 | 163 | 168 | 173 | 178 |

FEMALE.

| Age | 4 ft. 10 in. | 4 ft. 11 in. | 5 ft. | 5 ft. 1 in. | 5 ft. 2 in. | 5 ft. 3 in. | 5 ft. 4 in. | 5 ft. 5 in. | 5 ft. 6 in. | 5 ft. 7 in. | 5 ft. 8 in. | 5 ft. 9 in. | 5 ft. 10 in. |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 20 | 103 | 106 | 109 | 113 | 116 | 120 | 123 | 127 | 130 | 134 | 138 | 142 | 147 |
| 22 | 105 | 107 | 110 | 114 | 118 | 121 | 124 | 128 | 132 | 136 | 140 | 144 | 149 |
| 24 | 106 | 108 | 111 | 115 | 119 | 122 | 126 | 129 | 133 | 137 | 141 | 145 | 150 |
| 26 | 107 | 110 | 113 | 117 | 120 | 124 | 127 | 131 | 134 | 139 | 143 | 147 | 151 |
| 28 | 108 | 111 | 114 | 118 | 121 | 125 | 128 | 132 | 136 | 140 | 144 | 149 | 158 |
| 30 | 109 | 112 | 115 | 119 | 123 | 126 | 129 | 133 | 137 | 141 | 146 | 150 | 154 |
| 32 | 110 | 113 | 116 | 120 | 124 | 127 | 131 | 135 | 138 | 143 | 147 | 151 | 156 |
| 34 | 110 | 114 | 117 | 121 | 125 | 128 | 132 | 136 | 140 | 144 | 149 | 153 | 157 |
| 36 | 112 | 115 | 119 | 122 | 126 | 130 | 133 | 137 | 141 | 146 | 150 | 154 | 159 |
| 38 | 113 | 116 | 120 | 123 | 127 | 131 | 135 | 139 | 142 | 147 | 152 | 156 | 161 |
| 40 | 114 | 117 | 121 | 124 | 128 | 132 | 135 | 140 | 144 | 148 | 153 | 157 | 162 |

**Loss of Strength.**—Loss of strength, usually insidious in its onset, may first attract the patient's notice. Nervous disorders, neurasthenia, exophthalmic goitre, and other causes of general weakness, must be excluded. Slight loss of strength, especially when coupled with localizing symptoms, is, at least, suggestive.

**Cough.**—This is the most frequent early symptom and nearly always the one which first draws attention to the lungs. A slight persistent hacking cough, often dry at first, should receive careful attention. It often has periods of marked remission, so that the patient believes he is recovering from the "cold," and may give a history of "colds," repeated over a long period. A summer cough is always more suspicious than a winter cough, and it is not uncommon for a patient to have his suspicions first aroused when his cough, contracted during the winter, fails to disappear when the warmer weather sets in.

**Hæmoptysis.**—This is rarely the primary symptom and in nearly all cases a period of more or less pronounced ill-health precedes the so-called primary hæmoptysis. The first point to be considered when a patient complains of blood spitting is the source of the blood. Bleeding from the gums can be excluded by having the patient suck them at the time of blood spitting. Blood from the nasopharynx may be mixed with mucus, but usually some epistaxis is present. It may come from varicose veins at the base of the tongue or on the posterior pharyngeal wall. Bleeding from the larynx, unless it is seriously diseased, is of such rare occurrence that it need not be considered. A careful examination of the mouth, nose, and throat should always be made if any doubt exists. The amount of blood from these sources, when there is no epistaxis, is usually slight. It is rare for a hemorrhage of over one ounce to come from elsewhere than the lungs, stomach, or nose. Slight blood spitting following cough on several successive mornings is characteristic of hæmoptysis of tuberculous origin. It is rare in pulmonary tuberculosis to have a brisk hæmoptysis not followed by blood-stained sputum for a day or longer.

The bloody sputum should be fully examined. A uniform pink or bright-red, watery fluid, consisting almost entirely of saliva, comes usually from the gums or mouth and may be present for months. It should not be confused with wine, tobacco, prune juice, licorice, or medicine. Streaks of blood upon the mucus or upon masses of sputum usually come from the bronchi, and are not uncommon in bronchitis after severe coughing. Uniform pink, red, rusty, or darker (prune juice) viscid pellets, containing

minute air bubbles, occur in pneumonia (most common), heart disease, and pulmonary tuberculosis. Small purple or dark lumps without air bubbles which sink in water are usually due to heart disease. Pure blood in some amount, if it is frothy, is usually from the lungs, trachea, or bronchi, and if mixed with mucus or pus is unquestionably from the lungs. Dark blood and bulky clots are more usually from the stomach. The blood of hæmoptysis may be swallowed and then vomited.

When it is determined that the source of the blood lies below the larynx the next step should be to exclude all extrapulmonary disease which might cause hæmoptysis. Among these are ulceration of the trachea (rare), heart disease, aneurism, certain diseases of the blood (purpura, hæmophilia, scurvy, leukæmia, pernicious anæmia, the malignant type of some infectious fevers), atheroma of the pulmonary vessels, and abscess of the liver (perforating through the lungs).

Having excluded all sources of the hemorrhage except the lungs, these organs should receive due attention. At least 90 per cent. of all patients who have hæmoptysis develop at some later time pulmonary tuberculosis. Absence of physical signs is no proof of a non-tuberculous origin. Every patient who suffers from hæmoptysis of a drachm or more without a discoverable cause should be considered tuberculous until it is proved otherwise. The blood, and particularly any particles of pus or mucus, should always be examined for tubercle bacilli, which are found in a number of cases. The examination of the blood of hæmoptysis for tubercle bacilli may be greatly facilitated by hydrohæmolysis, the addition of 12 to 20 volumes of water (Nattan-Larrier and Bergeron) or of one-third volume of alcohol (Loeper and Louste) to the blood before centrifugalization. Slight general and local symptoms with an undoubted history of hæmoptysis justify a diagnosis of tuberculosis. Every patient who has suffered from hæmoptysis and in whom the diagnosis can be made in no other way should eventually be given tuberculin. Hæmoptysis may occur in bronchitis (especially fibrinous), bronchiectasis, gangrene, abscess, asthma, emphysema, acute lobar pneumonia, infarct, embolism, anthrax, syphilis, actinomycosis, parasitic diseases (echinococcus, distomum), tumors (carcinoma, sarcoma), in trauma of the lung or air passages, and in fact to a slight amount in nearly every pulmonary disease. The physical signs in these cases are usually well marked, and, furthermore, hæmoptysis in them is of rare occurrence. Several observers (Wolliez, Ollivier, Bach, Rosenbach, Lebant) have described a "nervous" hæmoptysis in the hysterical, but without tuberculin such a diagnosis cannot be made. Vicarious menstruation has not yet been proved to occur in normal lungs.

**Dyspnœa.**—Shortness of breath is sometimes the first symptom noticed by the patient, but it rarely occurs to such a degree that a physician is consulted in regard to it before other symptoms set in. In the absence of general weakness, of disease of the heart, and of the mediastinum, dyspnœa is usually due to pulmonary disease, and if this be of slight discoverable extent, the probabilities are that it is tuberculous. Unaccountable dyspnœa or a sudden attack of asthma is always suspicious.

**Pleurisy.**—Recent work has done much to prove that most idiopathic pleurisies are tuberculous. Pleuritic pain marks the onset of many cases of pulmonary tuberculosis, and it should never be forgotten that "pleurisy" is not a disease, but a symptom of several diseases. If other organic disease

can be excluded, the pleurisy should be considered tuberculous until the contrary be proved. A dry pleurisy at one apex or a double pleurisy without other cause is nearly always tuberculous. Even if tubercle bacilli cannot be found in a pleuritic effusion it is well to assume the patient to be tuberculous, and to treat him accordingly. A persistent feeling of pressure in the chest demands careful consideration.

**Physical Signs.**—The value of physical signs must not be overestimated. When the extent of disease necessary to produce physical signs is considered, it is not strange that many patients present only indefinite changes which may occur in health. Furthermore, when it is recalled that large central lesions can exist without discoverable physical signs, absence of physical signs is not astonishing. While this possibility must be borne in mind, it occurs rarely. Marked physical signs are not to be expected in early cases, and any change from normal may become evident only after repeated examinations. At least two examinations are necessary before the chest can be said to be normal in regard to physical signs. On the second examination those places should be first examined which were suspicious on the previous examination. For this reason it would be well to begin the second examination by auscultation over an area where changes were thought to be present at the time of the first examination, especially if these were the only abnormal physical signs.

Percussion yields little aid in some patients in early stages, but when the disease is of some duration its value is markedly increased. Slight differences should be checked by repeated examinations and after a full inspiration. Absence of dulness may occur even in advanced cases and hyperresonance should receive careful attention. The note may normally be slightly higher, pitched to the second rib, often more noticeable on the left side. Emphysematous changes may produce a relatively low note on the affected side. The right apex usually reaches a slightly lower level than the left, a point of no great importance. The movement of the bases of the lungs and the resonant areas above the clavicles must be carefully mapped out by percussion.

Auscultation undoubtedly yields the most trustworthy information and in many early cases it gives the only change in the physical signs. It should be practised before the patient is made to breathe deeply, and on a second examination the auscultation of the suspected area should be the first procedure. Slight changes in the breath sounds at the right apex are often difficult of detection. They are of more value if detected at only one apex, and if present at both the patient should be made to breathe noiselessly through his mouth, and the presence of stenosis of the larynx or bronchi by pressure from aneurism, tumor, enlarged glands, or traumatism excluded. Prolonged high or low-pitched expiration, or spluttering of the inspiration, suggesting fine crepitations which, however, cannot be heard, wavy breathing, weakened breathing, are all signs of great importance when limited to one apex. Wavy breathing must be carefully separated from the cardiorespiratory murmur. A venous murmur above one clavicle may suggest loss of vesicular murmur until the patient holds his breath. Some prolongation of the expiration may occur at the right apex in children, in thin, lanky women, and during forced respiration in many individuals. The vocal resonance, if equal on the two sides, indicates disease on the left. The whisper should *always* be auscultated over the entire chest, as in some instances it will first draw attention to the diseased area.

The change in breath sounds alone is rarely sufficient for diagnosis, but rales persistent or occurring on several examinations at one apex not due to influenza, and coupled with slight symptoms, border on certainty. Rales are more important than dulness and are frequently overlooked through failure to have the patient cough and breathe properly. They may be present one day and absent the next, to recur on the following day. They are more likely to be heard on damp days than on dry, in the morning on waking than during the afternoon. Iodide of potash, certain alkaline mineral waters, tuberculin, and menstruation may increase the rales, while excess of alcohol (Turban), certain drugs (balsam, tars, etc.), profuse sweating, or prolonged dry following damp weather may decrease the rales. A sonorous rale ending in a prolonged expiration is almost pathognomonic of pulmonary tuberculosis (Williams). Fine rales may be heard in the prone and not in the upright position, and Upham believes when lying on the affected side rales may be heard that otherwise escape detection. Cybulski's laryngeal crepitations (oral rales) occur usually too late to be of any diagnostic aid.

Extraordinary care must be exercised in differentiating various sounds heard in the normal chest from rales: (1) Skin friction sounds are often heard just after the stethoscope is placed upon the chest, and slight pressure applied to it as the patient begins to inhale. A second breath or cough before moving the stethoscope or dipping the bell in water or vaselin will often eliminate these sounds. (2) The sounds produced in the muscles may resemble a hum, a fine crackle, or, if one muscle slips over another, a snap or friction sound. Such sounds are usually heard on the back, most often on both sides, but may be limited to one, and call for much ingenuity and experience in differentiation from fine rales. (3) A sound produced on swallowing resembling fine rales may cause some confusion, but is easily prevented by a word to the patient. (4) Sounds produced in the stomach and intestines can be heard over the lower part of the lungs and seldom cause error. They are usually heard on the left side below the limit of pulmonary resonance. (5) The peritoneal friction rub is rarely a factor worth considering. (6) The shoulder friction seldom enters into consideration, but may be heard in some cases over the scapula and shoulder-joint and at times closely simulate a pleuritic rub. (7) The occurrence of rales in the normal chest is still a mooted point. Atalectatic rales unquestionably occur over the base of the lungs posteriorly, but these quickly clear up. No good proof of rales in the chest of a person in health up and about has yet been presented. In one case where only a few rales existed in the infra-axillary region on one side, the patient reacted to tuberculin, and several years later relapsed and had tubercle bacilli in the sputum.

The location of the physical signs is the most important point in diagnosis. Pulmonary tuberculosis usually attacks the apex first, and persistent physical signs localized in the apex of one lung should always be considered tuberculous until the contrary is proved. The opposite is true of physical signs at the pulmonary base. Primary basic tuberculosis may occur, but basic tuberculosis is usually secondary to an older apical lesion. A secondary tuberculous infection of a non-tuberculous basic lesion may take place. When this occurs the apex may be the primary seat of the infection. Non-tuberculous basic disease, according to Fowler, may be due to: (1) Collapse of the lower lobe caused by pleural effusion, followed by

absorption of the fluid and falling in of the lower part of the chest on the affected side. (2) Collapse from the same cause, followed by cirrhosis of the lung and bronchiectasis. (3) Empyema opening into the lung. (4) Hepatic abscess or hydatid cyst of the liver, communicating with the lung. (5) Collapse of the lower lobe from pressure on the main bronchi by growths or enlarged and infiltrated mediastinal glands, followed by bronchiectasis. (6) Diffuse gangrene of the lower lobe resulting from a communication through the bronchi with the œsophagus, either directly or through the medium of a softened bronchial gland. (7) Chronic pneumonia and bronchiectasis following on the impaction of a foreign body in one of the bronchi of the lower lobe. (8) Unresolved and chronic pneumonia of the lower lobe. (9) Bronchiectasis secondary to catarrhal pneumonia and collapse. This lesion is rarely found except in children.

Scattered rales over a side with bronchophony and without dulness or other signs are nearly always due to tuberculosis (Williams). This is also true of pleuritic friction sounds at one apex or on both sides in the absence of other causative factors. The pseudopleural friction rub of Rosenbach has been mentioned. In early childhood the resilience of the chest walls and the dissemination usually render diagnosis from bronchitis or bronchopneumonia difficult. Examination of the stools for tubercle bacilli should be made. In old age prolonged expiration, jerky breathing, and even a few dry rales are of less import than in adult life unless limited in area. Symptoms in these cases are of much importance.

Myoidema and the gingival line have no diagnostic value, but demand a careful pulmonary examination. Enlarged cervical glands or scars upon the neck and a persistent pallor of the palate or larynx are suggestive.

A change in the frequency of the pulse which occurs in tuberculosis when the patient assumes an erect posture is, as pointed out by Wells and Maclachlan, a point in differential diagnosis between tuberculosis and simple bronchitis. The pulse may have a lower tension than normal, but its increased frequency is the most important factor. The rate of the pulse observed by the physician in his office or even at the home of the patient is often of little value in diagnosis. A persistently high pulse without fever, coupled with loss of weight, is suggestive of tuberculous infection.

Neither physical signs nor symptoms alone are sufficient in many cases for diagnosis; but the combination of slight signs and symptoms will often definitely settle the matter. Slight or indefinite physical signs without symptoms are not sufficient to establish a diagnosis.

**Sputum.**—The rule to examine the sputum of every patient who has any respiratory affection, slight or serious, admits of no exception. Many cases are overlooked by failure to follow this. If the patient says he has no sputum, a specimen obtained by clearing the throat in the morning or after meals should be requested. The macroscopic appearance of the sputum is of little if any value, and the absence of tubercle bacilli in the sputum is no proof of the absence of pulmonary tuberculosis. One positive examination settles the diagnosis, but one negative examination is of little value. The presence of elastic tissue in the sputum is evidence of destruction of the pulmonary tissue. Tubercle bacilli may be absent on repeated examinations when the disease has become fibroid, but the absence of these bacilli when the lung is breaking down or has undergone extensive destructive changes is presumptive evidence that the disease is non-tuberculous.

Tubercle bacilli may be found in the sputum months before physical signs appear in the lungs. They undoubtedly find their way into the nasal and buccal secretions and have been discovered there in healthy individuals (Straus, Cornet, Jones). For this reason one tubercle bacillus is not sufficient for a diagnosis. In children or in patients who are suspected of swallowing the little sputum they have, a careful examination of the vomitus, stomach contents, a swab of the fauces, or of the fæces by Strasburger's method (mixing with water, sedimenting, mixing the top layer with three or four parts of 95 per cent. alcohol, centrifuging and staining the sediment) should be made. The expectoration of calcareous matter rarely if ever occurs except in tuberculosis of the lungs or of the bronchial glands. The inoculation of sputum into a guinea-pig will at times reveal tubercle bacilli that cannot be found by careful and repeated examination.

Potassium iodide in some cases undoubtedly increases the bronchial secretions, and in some instances tubercle bacilli while absent previously have been found in the sputum following its administration. Rales also appear after its exhibition and a few patients have become markedly worse after its use. These were, however, in all probability, simply coincidences. Its use in a number of cases has produced no harmful results in the writer's experience. Similar results are said to follow the use of certain alkaline waters. A cold pack to the chest overnight is said to increase the sputum and should be followed by a cold sponge and brisk friction in the morning. When no sputum can be obtained and the patients cough, it has been advised by Blume to have them cough for eight or ten mornings on large slides, which are then stained.

**Sputum Examination.**—The chief value of this is for diagnosis. Its prognostic importance has been greatly exaggerated and so far no practical method has been devised by which secondary infection can be accurately diagnosed. It is high time that the profession should cease to tell patients that they are improved or worse because fewer or more tubercle bacilli are found on the second examination, or in fact to inform a patient that his disease is severe or slight because many or few bacilli are found on the first and possibly the only examination. Wood, out of 1400 patients in the consumptive wards at the Cook County Hospital (Chicago), found that 120 (8.5 per cent.) did not have tuberculosis, but some disease which in a number of cases might have been at least improved by appropriate treatment. Nagel found tubercle bacilli in only 161 (15 per cent.) out of 1081 patients, in 1.4 per cent. of 762 patients in stage I (Turban), 38 per cent. of 264 in stage II, and in 90 per cent. of 55 in stage III. The diagnosis in most cases can be made, therefore, before tubercle bacilli appear in the sputum.

The *collection* of sputum for examination is very important. It is surprising how often tubercle bacilli occur in patients who have "no" sputum. The morning sputum should be obtained when possible and the specimen should always be coughed up from below, not drawn down from the nose. Patients with little sputum should be told to bring the little dense, tough balls they raise at infrequent intervals. These are often the only parts of the sputum to show tubercle bacilli, and great stress should be laid on their collection. Tubercle bacilli stain well in putrefying sputum after three months or longer. Water or carbolic acid should not be added to the specimen.

An initial hæmoptysis should always be examined for tubercle bacilli, and, if none are found, inoscopy or hæmolysis should be carried out. No sputum should be said to be free from tubercle bacilli until it is negative on at least three successive days, and the examiner is convinced that it has been carefully collected.

The *macroscopic examination* reveals in many instances little of value. Sputum in pulmonary tuberculosis has no pathognomonic macroscopic appearance. Early in the disease the sputum is largely mucoid, more or less transparent, and with an occasional fleck of yellow pus. As the disease advances it may become white, contains less air, and finally assumes a yellow or yellowish-green appearance, occurs in masses (nummular sputum), and sinks in water. As improvement sets in, the sputum becomes less yellow, then white, and finally consists of glairy mucus, which may persist for months and years. Macroscopic particles of lung tissue are occasionally found in the sputum and usually consist chiefly of elastic tissue. Lung stones are infrequent. Nummular sputum may occur in bronchitis.

*Quantity.*—This varies from the slightest trace to 800 cc. in twenty-four hours, but rarely exceeds 100 to 125 cc. a day. As a rule, in the earlier cases the sputum is small in amount, increases as the disease advances, and is seldom absent when symptoms have continued for two months or longer. While the disease is undergoing arrest, the sputum usually diminishes and finally disappears. In some cases it continues for years after tubercle bacilli can no longer be found. Sudden changes in the amount always call for a careful examination, as a sudden decrease sometimes occurs in acute miliary tuberculosis and has been observed in temporary heart weakness or intercurrent diseases. Miliary tuberculosis is at times ushered in with a sudden increase of the sputum. In many cases the morning sputum is the first to appear and the last to disappear. "Generally speaking it may be said that the character and amount of the sputum in phthisis depend upon the degree of implication or irritation of the bronchial or bronchiolar mucous membrane (especially of that of the larger bronchi), the extent and rapidity of the cavity formation, and the situation of such cavities in the lungs, and the nature and site of their communications with the bronchi" (Mackenzie).

*Odor.*—Fresh sputum may have a sickly, sweetish odor. The sputum is rarely foul, unless some complication has set in.

*Taste.*—Patients often note a slight salty taste, and those who have had hæmoptyses can often detect blood by the taste. In some instances the taste (or odor) is so sickening that the patient is nauseated and cannot take any nourishment for a time.

*Reaction.*—The sputum when fresh is practically always alkaline.

*Specific Gravity.*—This varies, but on an average may be said to be 1013 (Kossel). When the sputum sinks in water (less watery and foamy, and more solid), it indicates lessening of the secondary inflammation (Volland).

*Consistency.*—This varies from that of water to sputum so tenacious that it will remain in an inverted cup. The sputum ordinarily is moderately tenacious.

*Lung Stones.*—Chalky concretions are usually found in the sputum of chronic patients with rapidly advancing ulceration. Kidd believes that they are nearly pathognomonic of pulmonary or glandular tuberculosis. They are rather uncommon (16 among 1000 cases, Williams), and usually

occur singly from time to time (500 have been recovered from one patient).

Their size varies from that of a small shot to one as large as a cherry, so large it caused suffocation in a child. They are generally very irregular in form, with numerous rough projections and usually white. They are formed in the lungs and glands from calcification of caseous masses, and it is said "in obstructed bronchi," but this is to be questioned. They may occur at the time of hæmoptysis.

*Variations According to the Type of the Disease.*—In acute pneumonic phthisis the sputum is at first similar to that of acute pneumonia. Later it takes on a greenish tinge. Such a change in an unresolved pneumonia is always suspicious. Acute miliary tuberculosis of the lungs may occur without sputum. If secondary its onset may be marked by a sudden diminution of the sputum or by a change to a watery consistency and a marked increase in the amount. An attack of acute bronchitis may decrease the sputum temporarily to increase it later. In any sudden increase of the amount secondary organisms should always be carefully looked for.

*Microscopic.*—The examination of a fresh specimen may prove to be of value and reveal elastic tissue. In every case where tuberculosis is suspected from the symptoms and physical signs and no tubercle bacilli are found, careful examination of the fresh sputum should be made.

*Selection of Particles.*—Search should be made for the little flecks of pus or cheesy particles which are readily seen on a black background. Each slide or cover-slip should contain particles from five or six different parts of the specimen. The contents of tonsillar crypts may cause some confusion and may contain acid-fast bacilli.

*Cells.*—The cellular elements of the sputum include pavement epithelium, alveolar, ciliated, glandular, cylindrical, pus, red blood, and giant cells. In some cases the cells may be pigmented. The giant cells are best seen when the sputum is hardened in Zenker's fluid, sectioned and stained. In many specimens stained for tubercle bacilli, cells can be readily recognized. Eosinophiles are not absent from the sputum in pulmonary tuberculosis, as has been claimed, but are of no diagnostic or prognostic significance. Pigment cells with myelin occur as well as in health. The tubercle corpuscle of Lebert is a granular, dark-colored cell, probably alveolar in origin. Fat in bizarre forms has been found in fresh specimens.

*Elastic Tissue.*—Dettweiler's maxim, "Where elastic tissue is, there are also tubercle bacilli; indeed, the greater the number of fibers, the more numerous the tubercle bacilli," is still held in part, but its converse cannot be affirmed, as many specimens contain tubercle bacilli and no elastic fibers. Tubercle bacilli always occur first. Von Voornveld concluded, from a large number of sputum examinations, that when the number of tubercle bacilli exceeded "Gaffky V," elastic fibers were almost never absent. Elastic fibers are the surest sign of extensive destruction of pulmonary, bronchial, or tracheal tissue. The bronchial elastic tissue, according to Osler, forms an elongated network, or two or three long, narrow fibers are found close together. The fibers from the alveoli are often branched, and show the outline of air cells. The "coral fibers," described by Leyden and Engel, are no doubt elastic fibers with adherent fatty particles. In healing processes the elastic fibers first become scarce and finally disappear. Their constant presence shows advancing disease. They are absent in acute

processes until the walls of the bronchi are broken down; 90 per cent. of all cases in which elastic tissue occurs are said to be tuberculous.

Elastic fibers may occur for one or two years without signs of cavity formation. In a study of the sputum of 70 patients, Sokolowski found elastic fibers in 18 out of 19 patients with symptoms of destruction of pulmonary tissue; in 30 out of 40 patients with more or less consolidation, elastic fibers were present as well as in 8 out of 24 patients with very limited lesions.

Various crystals may be found in tuberculous sputum, and among them may be mentioned Charcot-Leyden, cholesterin, hæmatoidin, fatty, leucin, tyrosin, phosphate, and oxalate crystals. Fibrinous coagula, striking, tree-like bodies, may occur in phthisis as well as in fibrinous bronchitis. Casts of the bronchi also occur, and it is not very rare to find the blood coagulum after an hæmoptysis in the form of a cast of a bronchus. Caseous matter may be found.

*Tubercle Bacilli.*—The search for tubercle bacilli in the stained specimen is unquestionably the most important step in the examination of a suspected person. The stain consists of 1 part of saturated alcoholic (95 per cent.) solution of fuchsin, and 9 parts of 5 per cent. carbolic acid solution. Many new stains have been introduced, but none have stood the test of time like this. Either cover-slips or slides may be used, but on the whole slides are more satisfactory. Only new slides or slips should be used in specimens for diagnosis. The time required for staining varies with the degree of heat employed; the greater the heat to a certain point, the more rapid the staining. A small flame should be used, and the fluid brought just to a boil, or, better, until bubbles are seen to collect about the thicker parts of the smear. This heat should be kept up for one to five minutes, or until crystals of fuchsin are seen to appear on the surface of the fluid. As some hold that not one-half of the tubercle bacilli in a preparation are stained when it is examined, the great value of sufficiently overstaining is readily seen. In routine work much time is saved by using the "cold" method. This consists in immersing the preparations in the cold stain for twenty-four hours.

*Decolorization.*—Alkalies, other dyes, salts and alcohol, as well as acids, organic and inorganic, can decolorize specimens. Acid alcohol and Ebner's decalcifying fluid (HCl, $NaClO_3$, of each 2.5 parts dissolved in 100 parts of distilled water and 500 parts of 95 per cent. alcohol added) are excellent. (Tubercle bacilli resist this for ten or more minutes.) Rosenberger has advised the use of sweet spirits of nitre, an alcoholic solution of ethyl nitrite, as a decolorizing agent for the ordinary carbol-fuchsin stain. After staining five to ten minutes, the specimen is decolorized one-half minute in the spirits of nitrous ether, and counterstained. Smegma bacilli as well as the fatty granular particles decolorize in this. The author claims it does not injure tissue as sulphuric acid does at times; it is easy to prepare, keeps indefinitely, acts more quickly and surely than the ordinary decolorizing agents, and gives a clearer and better-defined field. By its use much thicker preparations can be used, and so more sputum can be examined at one time, an advantage of no little importance where the tubercle bacilli are few.

The tubercle bacilli are to be *well* stained in the first place and then carefully decolorized, controlling this step in important cases by frequent examinations under the low power of the microscope. This cannot be done if a counterstain is added to the decolorizing agent, and, therefore, Gabbett's solution (2 per cent. methylene blue in 25 per cent. $H_4SO_2$), so widely used,

should never be employed for diagnosis nor in any case for urine. For routine examinations in sanatoriums the use of Gabbett's solution is permissible after diagnosis, but is not to be recommended, as every specimen should be subjected to alcohol. Every specimen should be counterstained. Vesuvin has proved a good counterstain for violet-colored tubercle bacilli, and methylene blue (Loeffler's) or malachite green for red.

*Differential Diagnosis from Other Acid-fast Bacilli.*—The important point in the differential diagnosis of the tubercle bacillus lies in its resistance to decolorization not only by acids, but by alcohol. A large number of "acid-fast" bacilli have been found, but so far none resists alcohol to the same extent as the tubercle bacillus. Alcohol, therefore, should always be used in decolorization. The only absolutely certain method is to control the decolorization by subjecting tubercle bacilli placed on the same cover-glass or slide to exactly similar manipulations. The majority of the acid-resisting bacteria grow readily and quickly on the usual media, often at room temperature. Inoculation of guinea-pigs may have to be employed. In most instances these bacilli differ morphologically from the tubercle bacillus, and are usually longer or shorter and broader. They occur in butter, milk, smegma, contents of tonsillar crypts, cerumen, nasal secretions, in the sputum of some cases of gangrene, bronchiectasis, putrid bronchitis, in manure, and on timothy hay, and, according to Lustgarten, in syphilis.

*Examination.*—This should be done systematically and thoroughly with a mechanical stage, and at least two preparations from each specimen should be examined. Much time can be wasted by counting tubercle bacilli in the preparations, but a schema such as that devised by Gaffky is of considerable value in comparing the findings from time to time. It is as follows:

1. Only 1 to 4 bacilli in whole preparation.
2. Only 1 bacillus on average in many fields.
3. Only 1 bacillus on average in each field.
4. 2 to 3 bacilli on average in each field.
5. 4 to 6 bacilli on average in each field.
6. 7 to 12 bacilli on average in each field.
7. Fairly numerous on average in each field.
8. Numerous on average in many fields.
9. Very numerous on average in many fields.
10. Enormous masses on average in many fields.

In this method a No. 3 ocular with 16 mm. tube length and $\frac{1}{12}$ oil-immersion lens should be used. The fallacy of basing any conclusions upon the number of bacilli is readily seen when the uncertain distribution of bacilli in the sputum is kept in mind. A number of methods have been devised to determine accurately the number of bacilli, but they are of little practical value.

A careful study of the sputum of 259 cases at the Adirondack Cottage Sanitarium showed that when the diagnosis was made before tubercle bacilli were present in the sputum, *i. e.*, before ulceration had begun, the chances for recovery were at least twice as good and on the whole seemed many times better; that only 44 per cent. of the patients with tubercle bacilli on admission had lost them on discharge after a residence of about five months; that the number of bacilli seems to vary on the whole directly with the severity of the case; that if the number of bacilli steadily decreases in a series of examinations at intervals sufficiently long, the patient may be

improving, but the constitutional symptoms and local signs are much more trustworthy; that if on repeated examinations large numbers of bacilli are found, the disease has in all probability advanced to cavity; that the morphology of the tubercle bacillus affords little or no ground for prognosis, but the short bacilli are suggestive of a more active process; and that the arrangement of the bacilli in clumps may occur in all, but is more apt to be found in the severer cases. These observations were based on a study of two preparations from each of a number of specimens in every case. The presence of few and many bacilli alternately indicates a cavity which opens and closes (Brieger). Mackenzie thinks many bacilli in non-purulent sputum betokens a bad prognosis.

Splitter sputa, fine, generally long granules, arranged in a row or in groups, Spengler believes are involution forms of tubercle bacilli and may be found when no "normal" tubercle bacilli can be seen. Such sputum is not always infectious to guinea-pigs. The tubercle bacilli usually occur free, but may be found in pus or alveolar cells. Denys and other observers have noted this phagocytosis in the polymorphonuclear leukocytes, but Loewenstein and Allen have endeavored to connect it with prognosis. Loewenstein found it present in 10 per cent. of all patients, while Allen saw it at least once in 82 per cent. of all patients, and in 59 per cent. observed it several times.

*Secondary Organisms.*—It can be safely said that a diagnosis of secondary infections on account of the rapid growths of these organisms cannot be made from sputum examined several hours after expectoration. The mouth should be thoroughly cleansed before collecting the specimen and the sputum, not later than fifteen minutes after it is expectorated, should be carefully washed in three to six changes of distilled water. The mass should then be torn apart and a piece of sputum from the middle of the mass examined. Secondary infection should be diagnosed only after repeated examinations, and even then so many errors may creep in that clinical symptoms have often to be relied upon.

In the ordinary examination of sputum, streptococci, staphylococci, diplococci, torulæ, sarcinæ, and bacilli, singly, in chains, or in zoöglœa masses, occur more or less frequently. The *Micrococcus catarrhalis* (Pfeiffer), a biscuit-shaped diplococcus resembling the gonococcus, is common. The pneumococcus is less frequent. The influenza bacillus is probably, next to the cocci, the most important organism of secondary infection. After an epidemic this bacillus can lurk for months in the lungs and may start afresh a quiescent tuberculous process. The diagnosis by the culture method is not as certain as the method of staining described by Lord.

*Methods for Increasing the Number of the Tubercle Bacilli in the Part of the Specimen to be Examined.*—When no tubercle bacilli can be found in a suspected case various methods have been devised to make the search more accurate. The one most frequently employed is to render the sputum more or less homogeneous and then to sediment or centrifugalize it. An equal volume of 0.2 per cent. NaOH is added to the sputum and the mixture is boiled, stirring, if necessary, until the sputum is dissolved. It is then neutralized with 10 per cent. acetic acid, using phenolphthalein as an indicator. The fluid is then sedimented or centrifugalized. Another method is to use equal parts of Javelle water (potassium hypochlorite) and sputum. After shaking at intervals for fifteen to thirty minutes the solution is freed of chlorine, by the addition of a little normal sodium or potassium. Digestion

with pancreatin in a slightly alkaline solution for twenty-four hours or longer yields good results. Vigorous shaking with 9 parts of 5 per cent. carbolic-acid solution and 1 of sputum, followed by centrifugalization or sedimentation, is useful. A fixative such as egg albumen or some of the original sputum must be used with these methods. Inoscopy has been successful in some cases.

Another procedure which has given less satisfactory results is the "enriching" of the specimen. In ordinary sputum at room temperature or even in the thermostat, little or no evidence of increase of the tubercle bacilli can be found. The addition even of some culture medium to the sputum seems to aid little in the growth of the tubercle bacillus. Making a culture from the interior of a piece of sputum thoroughly washed, on blood serum or brain agar, or planting first on gelatin plates and then replanting on blood serum from parts of the plate apparently sterile, may aid in diagnosis. Dilute formalin affects the growth of acid-fast bacteria less than that of some other forms. An emulsion is made of the sputum and a few drops of formalin added. At different intervals beginning at ten minutes, tubes are inoculated and pure cultures of the acid-fast organism may be obtained in some. A marked increase in the number of these organisms at 30° C. in ordinary bouillon is conclusive proof that the organism is not the tubercle bacillus.

Several years ago Strassburger suggested in the examination of the stools for tubercle bacilli, diluting and sedimenting first with water and then with alcohol. This decreases the specific gravity of the fluid and so hastens sedimentation. The examination of the stools may be of special value in children and women.

*Injection into Animals.*—Sputum in which no tubercle bacilli can be found, which on inoculation produces no tuberculosis in four to six weeks, contains no tubercle bacilli. The sputum should be injected, as soon as possible after it has been collected, subcutaneously in the groins of two guinea-pigs and the animals examined from time to time for enlarged inguinal lymph glands. At the end of four to six weeks the animals should be killed and any enlarged glands thoroughly examined for bacilli or for tubercles, both macroscopically and microscopically. The injection and autopsy should be so performed as to avoid any possible chance of contamination. Subcutaneous injection of sputum is less likely than intraperitoneal injection to produce death from the effect of other organisms. Intraperitoneal inoculation is thought by some to be more sensitive than subcutaneous. Subcutaneous injection may be made in the leg at the level of the knee. Nattan-Larrier advises inoculation into the mamma of a guinea-pig, one or several days after delivery. Tubercle bacilli are said to occur in the milk on the fifth to the tenth day. Heating the sputum to 60° C. for ten minutes may destroy many secondary organisms which may be virulent for the guinea-pig without affecting the tubercle bacilli. Pseudotubercle bacilli can produce tubercles, but cultures readily separate the two forms. To attempt to determine the virulence of a strain of tubercle bacilli by injection of animals with sputum is futile, as the number of bacilli in the injection cannot be controlled.

Recognizing the frequency with which the lung is punctured in suspected pleuritic effusion and recalling how infrequently untoward results occur, Henkel has advocated aspiration of the pulmonary juices at the seat of the

lesion and examining them for tubercle bacilli. The method is not to be recommended.

*Chemistry.*—The nitrogenous matter lost in the sputum is 3.8 per cent. of the total nitrogenous output in a well-nourished man and 6 per cent. in a fasting man. Glycogen and urea have been found in the sputum, as well as a digesting ferment and, in diabetes, sugar. Wanner has found the albumin, which is absent in bronchitis, in general proportional to the extent of the lesion (from which it comes) and the mucin less in amount than in chronic bronchitis or pneumonia. Other organic substances said to be found in sputum are nuclein, peptone, and protargon. Most of these observations hold only for the sputum of advanced cases. Albumin occurs as serum albumin, myosin, and globulin. Marcet has found in health that potassium was excreted in the sputum as a carbonate, in pulmonary tuberculosis as a phosphate. Among other constituents have been noted nuclein, lecithin, cholesterin, soap, free and combined fatty acids, and Cl, S, P, K, Na in various combinations with Ca, Fe, Mg, and Si. Ammonia and sulphuretted hydrogen occur as decomposition products.

**Urine.**—The urine is of slight value in diagnosis. The diazo reaction occurs only in some advanced cases. Albuminuria is exceedingly rare in incipient cases. Polyuria is uncommon.

**Cytodiagnosis.**—It has been suggested to blister and to examine the exudate. If the eosinophiles in a differential count fall much below 8 per cent., pulmonary tuberculosis is said to be suggested.

**Tuberculin.**—Tuberculin should be used diagnostically only as a last resort. When a patient with suspicious symptoms, with indefinite physical signs and with no tubercle bacilli in the sputum on repeated examinations, wishes a positive diagnosis, tuberculin should be administered.

The best form to be used for diagnostic purposes is the old or original tuberculin of Koch. Some other forms are many times more powerful, but they have up to this time been neither so carefully investigated nor have many systematic attempts been made to standardize them or to determine the dose at which healthy individuals react. For these reasons it is well to use only the old tuberculin for diagnosis. The strength of this tuberculin is far from constant even when prepared by the same method and from the same strain of tubercle bacilli. It should always be standardized by comparison with tuberculin of a known strength before use. Meyer has used the bacillary emulsion for diagnosis in 28 patients, with positive results in 25, 18 of whom showed at some later date tubercle bacilli in the sputum. His initial dose was 0.0025 mg. (solid substance), then 0.005 and finally 0.012 or 0.024 mg.

**Dosage.**[1]—The dose necessary to produce a reaction in a healthy individual varies considerably with the tuberculin used. Prepared according to Koch's directions and properly standardized by Otto's method, it may safely be stated that 0.010 cc. of the original tuberculin never produces a typical reaction in a normal person. For an adult 0.0005 cc. is a safe initial dose, but in many cases it is not necessary to give less than 0.001 cc., although it is often best to give first 0.0001 or 0.0002 cc. If no reaction occurs the following doses should be given: 0.001, 0.003, 0.005, and 0.008 or even 0.01 cc. It is well always to repeat the last dose. Some advise a single large dose for fear that repeated small doses may produce some immunity, and affirm that

[1] In O. T. and B. F 1 cc. = 1 gm.; in B. E. and T. R. the dose is stated in amounts of the solid substance

no higher reactions occur in a susceptible individual from a dose of 0.005 to 0.010 cc. than from 0.001 or 0.002 cc. The observations of the writer do not bear this out.

The general condition and build of the patient, together with the duration and extent of the disease, must be considered in the dosage, as well as the age in children. In children, 0.0001 cc. is a safe initial and 0.003 cc. a safe maximal dose. Loewenstein recommended the use of small doses, 0.0001 cc., or 0.0002 cc. repeated three or four times. In 180 patients, 87 per cent. reacted on the first, second, or third injection of this small dose. Failure to react to five similar doses was noted in 8 patients who, however, reacted to 0.002 to 0.010 cc. with unusual severity (Loewenstein). Of 6 patients in the writer's experience, 3 failed to react to four doses of 0.0002 cc., and 3 reacted, 1 on the first, 1 on the second, the third on the third injection, while the 3 who failed to react to these small doses all reacted to larger ones.

This method, Loewenstein holds, indicates the degree of susceptibility to the tuberculous poison. Non-tuberculous individuals, he believes, would react to this same dose, repeated often enough. From a limited experience with this method it would appear that patients who react suffer as severely as those who are given larger doses, and the fact that the larger doses must in some cases be eventually administered prolongs the test considerably. Roth-Schulz begins with 0.0005 cc. and never exceeds 0.0025 cc., often repeating the same dose two or three times. Nagel found that 164 (27.5 per cent.) of 597 tuberculous patients reacted first to 0.010 cc. Roepke obtained as many reactions with the scale of 0.0002, 0.001, 0.005 cc. as with an increase from 0.001 to 0.005 to 0.010 cc.

**Method of Administration.**—In order to measure the dose, the tuberculin must be diluted, preferably by the physician. This is best done by means of a pipette, graduated to read to hundredths of a cubic centimeter, and a graduated cylinder. A solution of 0.25 per cent. phenol in physiological salt solution is the best diluent, but either may be used alone. The phenol solution may be kept one week in a dark, cool place, but a solution in normal saline should be freshly prepared for each injection. The hypodermic syringe should be carefully sterilized, preferably by boiling, as well as all pipettes and cylinders. The needles may be kept in alcohol (95 per cent.). It is sufficient to cleanse the skin thoroughly with 95 per cent. ethyl alcohol before and after the injection, which is best made subcutaneously in the subscapular region, avoiding areas of induration produced by previous inoculation. The reaction usually occurs in eight to twenty hours, and it is well to administer the tuberculin during the evening or late afternoon. It may occur earlier (in four hours) or later (in thirty-six hours), and possibly, if very slight, be obscured by sleep, but this must be of rare occurrence. The temperature of a patient should be taken every two hours while awake for several days (at least two) before the tuberculin injection and carefully recorded.

The patient should be kept quiet on the day of the injection, but not necessarily in bed. If given in the evening the patient is usually kept in bed the following day and until noon on the succeeding day, as occasionally a retarded reaction occurs. The main advantage of rest is the avoidance of every possible cause that may influence the reaction. Theoretically the patient should be under the same conditions before and during the test.

The temperature should be recorded for two or three days after the reaction. If the patient fails to react, the second dose should be given on the evening of the second day following, and the other doses repeated at the same interval. Three days may elapse between doses. If an indefinite reaction occurs with a slight rise of temperature, it has been advised to repeat the injection the day following the first. On account of delayed reactions this procedure should be followed with some reserve.

Other methods of administration have been suggested. Freymuth has administered tuberculin by mouth in capsules soluble only in alkaline fluids, but obtained unsatisfactory results. In v. Schroetter's clinic, and in a few instances by Moeller and others, tuberculin has been administered by inhalation (Bulling's atomizer). It is stated that the dose required must be thirty times as strong (30 mg. for an active, 250 mg. for an inactive or latent process) and that reaction to a small dose indicates disease of the lung proper. This work has not been confirmed.

**Contra-indications.**—Tuberculin should not be used when a patient's oral temperature reaches 100° at any time of the day. The objections of Koch and others to the use of tuberculin in patients who have not an absolutely normal temperature have not been upheld in the writer's experience. In patients with extensive physical signs it should be employed with the greatest care. It should not be administered to patients with night-sweats, great dyspnœa, recent hæmoptysis (within a month), general glandular involvement, meningitis, heart disease, nephritis, epilepsy, etc. Exceptions may under certain conditions be made in regard to nephritis and general glandular involvement. Tuberculin should never be used after acute diseases nor for two or three weeks at least after a febrile attack of unknown cause. In some neurasthenic and hysterical patients the insertion of the needle will cause a rise of temperature. A preliminary injection of distilled water should be given, and it is wise to refrain from a discussion before patients of the symptoms that may occur during the reaction.

**Reaction.**—In a typical tuberculin reaction the patient begins to feel indisposed about eighteen hours after the injection. This rapidly becomes more marked and he is soon willing to go to or remain in bed. Severe headache, general malaise, pain in the back and limbs, a slight tendency to (increased) cough, loss of desire for food, in some cases nausea and vomiting, and in severe reactions profound prostration occur. The temperature often rises to 101°, but may not reach more than 100° or may go to 107° without apparent ill results. Much importance has been attached to an increase of the physical signs in the chest (local or "organ" reaction), but no perceptible change occurs in a large number of early cases. The absence of these changes is no proof that a reaction has not occurred. When changes occur they are such as are produced by hyperæmia in the tuberculous areas, *e. g.*, rough breathing, wavy inspiration, crepitations, and possibly a slightly higher percussion note. Tuberculous glands or joints may show marked local reactions. The same is true of the larynx. A well-marked local reaction, even in the absence of a general reaction, including fever, is held by some to be conclusive of tuberculosis. The day following an ordinary reaction the temperature is again normal and the slow fall is rarely seen except in charts where the temperature has been taken throughout the night. In some cases, and even where the temperature is not high, the period of elevated temperature extends over two or even more days.

Herpes labialis is not uncommon during severe reactions. The swelling, redness, and pain at the site of injection vary greatly, and may be quite severe, but never proceed to suppuration if asepsis has been preserved. Gangrene at the site of injection occurred in one of Koehler's patients, due, it was found later, to contamination of the diluent with sulphuric acid.

Among other symptoms more or less inconstant are faintness, giddiness, insomnia, somnolence, fatigue, restlessness, stimulation (rare), weakness, and localizing symptoms, *e. g.*, oppression in the chest, increased expectoration, dyspnœa, and pleurisy (rare). Other foci of tuberculous disease may be discovered by localizing symptoms in the glands, bones, joints, bladder, etc. Marked general and localizing symptoms even with slight rise of temperature (1°) following 0.003 cc. or less of tuberculin may be considered as a positive reaction. A rise of 1.5° to 2° is considered by many essential. When large doses (0.008 or 0.010 cc.) are used, the reaction, to be conclusive, must be typical. A reaction to a small dose is held by some, but with little evidence, to be more conclusive than a reaction to a larger dose, even if this be well within the limit at which a healthy individual reacts. A second reaction to the same small dose, or a reaction following a repeated small dose, is held to be more characteristic. Rise of temperature or other symptoms immediately following the injection, or a rise of temperature, slight on the first or second day, more pronounced on the third, is not to be attributed to tuberculin.

The sputum may be increased in amount and more purulent. In a number of instances tubercle bacilli have been first found just after or during a reaction. This has never occurred in the writer's experience, although careful examinations have been frequently made.

The urine shows a marked diazo reaction in a number of instances. If vesical or renal tuberculosis be present, blood and pus as well as tubercle bacilli may occur. More albumose has been found in the urine than was injected (Kobler and Lenoir). Transient albuminuria is not frequent. Hæmoglobinuria, urobilinuria, peptonuria, hæmaturia, and increase and decrease of the amount of the urine and of its salts have all been described.

The changes in the blood are not constant and show no relation to the severity of the reaction, as manifested by the temperature and general condition. The erythrocytes are little affected, but the leukocytes are usually increased. A leukopenia may occur. Tubercle bacilli have never been proved to occur in the blood following a reaction. Virchow held that tuberculin caused dissemination, but later admitted that all changes found at necropsy after the use of tuberculin occur also in cases where it has not been used. Those who have had most experience with tuberculin have failed to note any dissemination of the disease from its use in man or in animals (Koch, Trudeau, Beck, Moeller, Baldwin, Petruschky, etc.). Many of the unfavorable results may be explained as coincidences. A patient at the Adirondack Cottage Sanitarium had an attack of hemiplegia from an old endocarditis, while the advisability of the use of tuberculin was being discussed. Another, who was refused tuberculin, developed an acute fibrinous pleurisy. Latham reports 3 such instances and Brieger 1. Convulsions have been noted in 1 case (Emerson), due possibly to hyperæmia of the brain. Distressing swelling in the trachea and larynx is exceedingly rare. The untoward results following tuberculin may in practically all cases be attributed to faulty doses or unwise selection of patients.

*Results and Statistics.*—The most important point to be established in regard to the tuberculin reaction is its specificity. Does the reaction occur in diseases other than tuberculosis, does it always occur in tuberculosis, and can other substances produce a typical reaction in the tuberculous? It must be borne in mind at the outset that a tuberculous focus in any part of the body may produce a reaction and in a suspected pulmonary lesion a reaction is not proof conclusive without further evidence, *e. g.*, symptoms of local reaction, of pulmonary tuberculosis. Undoubted proof exists that all cases of pulmonary tuberculosis do not react to tuberculin. Healed or completely encapsulated foci are said not to react, though many cases of surgical tuberculosis react long after they have been pronounced "cured." In some advanced cases with tubercle bacilli in the sputum the injection of tuberculin has failed to produce a reaction. Farther than this little proof has been adduced to show that tuberculosis fails to react to suitable doses of tuberculin. No case of early or incipient pulmonary tuberculosis has yet been shown to fail to react to a dose of 0.010 cc. or less of old tuberculin. The small percentage of instances in cattle of negative findings at postmortem after a positive tuberculin reaction may be readily explained, where no microscopic study is usually made. Madison's case of a positive reaction with negative findings may be thrown out, for the patient had a temperature varying from 100° to 102° before the injection. Warthin's recent experience, where tubercles were found on microscopic examination in the liver of patients who presented no other evidences of tuberculosis, may explain two cases of positive reactions in patients who died shortly afterward and no signs of tuberculosis were discovered at autopsy. An apparently healthy individual (without symptoms and physical signs) reacting to tuberculin need not be subjected to treatment for tuberculosis.

In experimental tuberculosis (guinea-pigs) the tuberculin reaction appears first eleven to thirteen days after inoculation (Moeller). Many substances, such as nuclein, albumin, peptone, diuretin, succinic acid, and various bacterial proteins, when given in doses much exceeding those of tuberculin, cause reactions in tuberculous patients similar in many respects to those caused by tuberculin. Peptone, for instance, is said to be no more dangerous than tuberculin, and as accurate (Freymuth). Normal saline and a solution of 0.5 per cent. NaCl and 1 per cent. $Na_2SO_4$ in distilled water (20 cc. subcutaneously) cause reactions (Sirot, Hutinel) in some tuberculous patients, and have been suggested for use in the place of tuberculin. Others, however, have failed to obtain reactions (Cabot), and say that these substances are not entirely innocuous.

Many diseases other than tuberculosis are said to react to tuberculin. It is a strange fact, however, that in spite of the many opponents to tuberculin, so few authenticated necropsies have been adduced to uphold this view. Many cases that have been reported as examples of other diseases reacting to tuberculin prove on investigation to be of little value and in some cases may be used as arguments on the opposite side. So far no case of syphilis, actinomycosis, leprosy, or chlorosis which reacted to tuberculin has been proved at postmortem to be free from tubercle.

Marmorek's early tuberculin reaction has been confirmed only by Nattan-Laurier. A guinea-pig is injected with the suspected fluid and in one-half hour "$\frac{1}{10}$ drop" of pure tuberculin is injected intracranially. A greater rise of temperature is noted in the injected animal than in the control.

Mérieux (Lyon) obtains serous fluid from a blister, blood serum, urine, or expectorated blood from an individual suspected of being tuberculous, and by injecting it into a tuberculous guinea-pig obtains an "indirect tuberculin reaction" if the patient be tuberculous. Brion could not confirm these experiments and thinks the procedure of no value in diagnosis, while Baillou's experience with 9 tuberculous and 9 non-tuberculous patients upholds it. The ophthalmic test, dropping 2 to 5 mg. of precipitated tuberculin, redissolved in normal salt solution, into the eye has been suggested by Calmette and others. It produces hyperæmia of the conjunctiva, especially in the caruncle, in from three or four to twenty-four hours, without general disturbance or aggravation of symptoms, and lasts twenty-four or even if severe seventy-two hours. No control of this test with tuberculin has yet been made. Von Pirquet's method of rubbing tuberculin into the slightly abraded skin and thus producing in tuberculous individuals a postule, which appears in two weeks, also needs confirmation to be of value.

**The "Opsonic" Index.**—This varies in health between 0.8 and 1.2. An index persistently above or below these figures or fluctuating above and below normal indicates tuberculosis according to Wright and his school. Ross has stated that he has never found an index of 1.3 in a patient not definitely tuberculous. The index should be noted during rest and on several successive days.

**Serodiagnosis.**—The agglutination of tubercle bacilli in homogeneous cultures (Arloing and Courmont) or in emulsions (Koch) by the blood serum has not been found to be of much practical importance.

**Roentgen Rays.**—Except in the hands of an expert the *x*-rays may prove to be of little help. Lessened excursion of the diaphragm on the affected side, attributed to loss of contractibility of the lung, diaphragmatic pleurisy, pressure on the vagus at the affected apex, or to some as yet unknown cause, often occurs early and requires little experience to measure accurately. It is best noted just outside the nipple line. The normal excursion on quiet breathing is 1.25 cm. (Williams). In a study at the Adirondack Cottage Sanitarium of 41 patients to compare the relative value of radioscopy, percussion, and inspection, it was found that radioscopy and percussion were of nearly equal value and more accurate than inspection. The heart is said to be drawn slightly toward the affected side, particularly during deep inspiration. Deep-seated foci may escape detection by physical examination and be easily detected by the fluoroscope. Considerable experience is necessary to detect slight changes in density, but a diagnosis can be made in patients without physical signs and without sputum. Some stress has been laid upon differences in illumination at the end of deep inspiration.

A diagnosis of pulmonary tuberculosis and emphysema may replace one of the latter disease, and a complicating emphysema hitherto unsuspected may be discovered by means of the *x*-rays. It helps similarly in "bronchitis." In acute miliary tuberculosis it shows some abnormalities of the lungs. Many claim that it always reveals pulmonary tuberculosis as soon as it can be diagnosed by any other means, but Williams records two patients with pulmonary tuberculosis and a negative *x*-ray examination. Skiagraphy, especially when the exposure has been but for some seconds, is of great value in the hands of an expert.

**Diagnosis of Special Forms.**—When once the diagnosis has been made, the physical signs, except on repeated examinations, help little in

differentiating the acute, subacute, or chronic forms of the disease. To separate these forms most reliance must be placed upon the history and symptoms which alone in nearly every instance will determine whether the disease is acute, subacute, chronic or arrested by the presence or absence, more or less continuous, of fever, night-sweats, emaciation, weakness, hæmoptysis, dyspnœa, cough, and expectoration. The physical signs reveal the damage that has been done, the symptoms whether it is progressing. In a few cases however, the disease advances so slowly and with so few pronounced symptoms that only careful examinations repeated at long intervals will reveal its slow advance.

**Acute Form.**—This may occur primarily or be engrafted upon a subacute or chronic type. If secondary, the high temperature, either continuous, remittent, or hectic, the rapid pulse, the hurried respirations with possibly an increase of cough and expectoration, and in some instances considerable cyanosis, all indicate an acute exacerbation. In a certain number of cases in this group the physical signs remain unchanged for some days.

**Latent Form.**—Every known method at times has to be employed to settle the diagnosis in these cases. The physical signs may be very indefinite and the symptoms only those of slightly failing health. Tuberculin alone makes the diagnosis in a large majority. In other cases the symptoms only are latent and on examination extensive physical signs are found.

**Early Form.**—In a considerable number of these cases the sputum contains tubercle bacilli, and while the symptoms may be pronounced the physical signs are often very indefinite. The diagnosis depends in many cases, when the sputum is negative, upon the typical symptoms, the absence of any other causative factor, and, finally, upon the tuberculin test when necessary.

**Advanced Form.**—In a few cases in this group the diagnosis is far from easy. The marked physical signs, usually most advanced at the apex, and the typical symptoms render the diagnosis easy in most instances, but in some types of chronic fibroid phthisis where the expectoration is abundant the tubercle bacilli may be very difficult to discover, and only at postmortem can it be definitely separated from chronic pneumonia. In some advanced cases with tubercle bacilli no reaction is obtained with tuberculin. Great care must be exercised if tuberculin is given to patients with extensive pulmonic changes. Most of the general and local symptoms are present, and in many instances tuberculous complications in other organs aid in the diagnosis. The presence of the tubercle bacilli is the best criterion.

**Differential Diagnosis.**—Pulmonary tuberculosis is protean in its early manifestations. Many and various diseases have been mistaken for it, and, what is in many instances more important for the patient, pulmonary tuberculosis has been mistaken for some other disease. We can accordingly divide the following diseases into two groups: First, those which pulmonary tuberculosis may simulate, and, second, those which simulate it.

Under the first group belong malaria, typhoid fever, nervous dyspepsia, chlorosis, neurasthenia, and many pulmonary affections, such as simple bronchitis, influenza, idiopathic pleurisy, asthma, and acute and chronic pneumonia.

In the second group are latent suppuration, including endocarditis and pyorrhœa alveolaris, pernicious anæmia, exophthalmic goitre, and a number of pulmonary diseases, including influenza, bronchiectasis, pleurisy with effusion, gangrene, abscess, parasitic diseases, actinomycosis, tumor, and

pulmonary infarct. The following differential points are of importance: A case of suspected malaria without the plasmodium in the blood after repeated examinations, with irregular chills and fever and which resists quinine, is usually not malaria. In such a case the lungs and sputum, if present, must be repeatedly examined. Bronchitis rarely complicates malaria.

Acute pulmonary tuberculosis may closely resemble typhoid fever. The onset is very similar, and an initial bronchitis may occur in both. The temperature curves may show a continuous high fever, but oscillations are more apt to occur in pulmonary tuberculosis. Profuse expectoration may occur in typhoid fever. An important point is the cyanosis, which is more frequent in acute pulmonary tuberculosis. The Widal test, if the patient has not had typhoid recently, may aid. The diazo reaction may occur in both.

Nervous dyspepsia is usually afebrile, causes little loss of weight, and complete anorexia is not usually present. Nervous dyspepsia, especially if occurring with a "stomach" cough, demands an investigation of the lungs and sputum.

Chlorosis is now less often considered a primary anæmia than formerly. Tuberculin should be injected in all suspicious cases or in those that fail to respond to a course of iron. Many patients with chlorosis are really cases of early pulmonary tuberculosis. Neurasthenia in a mild form should always recall the insidious onset of pulmonary tuberculosis.

Persistent simple bronchitis is rare before the age of forty. Bronchitis occurs more frequently in winter, the fever is of short duration, dulness on percussion is absent, and the rales are diffuse. However, a patient convalescing from a sharp attack of bronchitis may present rales in one apex for a short time. Emphysema, common in chronic bronchitis, is rare in pulmonary tuberculosis unless the lesion is advanced.

Bronchitis with physical signs limited to one side may be due to influenza, but this should be diagnosed in the absence of tubercle bacilli only when the influenza bacillus is found.

Bronchopneumonia in an adult should be considered tuberculous even when sputum is absent. A tuberculous bronchopneumonia in children shows higher and more irregular pyrexia, more rapid and profound emaciation, and more pronounced sweating. Bronchopneumonia due to streptococci may show night-sweats, loss of weight, cough, intermittent fever, dulness and rales in the upper lobe. The diagnosis in these cases rests solely upon the sputum examination. Chronic pneumonia, rather rare in occurrence, can be diagnosed only by exclusion and after many negative sputum examinations. It is rare in tuberculosis to find advanced disease limited to one side. In some chronic tuberculous cases, tuberculin may fail to produce a reaction. In simple chronic pneumonia the lesion is most pronounced at the base, in tuberculosis at the apex. The discovery of influenza bacilli or streptococci in a sputum repeatedly negative for tubercle bacilli bespeaks a chronic pneumonia. The number of cases of idiopathic pleurisy is reduced each year as more exact methods for the detection of tuberculosis are introduced. Pulmonary tuberculosis may attack an asthmatic, and asthma may set in early in pulmonary tuberculosis. It not infrequently follows an arrest of the tuberculous disease. The absence of tubercle bacilli and of localized changes separate the two diseases.

Latent suppuration in the abdomen or elsewhere may produce enfeebled breathing in the lungs, and many of the general symptoms of pulmonary tuberculosis. A leukocytosis should arouse suspicion and a careful examination may reveal a suppurating focus in the appendix, tube, gall-bladder, or elsewhere. Localized empyema is usually basic and sputum is generally absent. Slight persistent fever from pyorrhœa alveolaris may strongly suggest pulmonary tuberculosis in the absence of all other causes. Subacute endocarditis has been treated for months as pulmonary tuberculosis. The absence of changes in the lungs, the cardiac lesion, and the leukocytosis settle the diagnosis.

Hodgkin's disease with slight glandular involvement, high fever, prostration, and emaciation may closely simulate acute miliary tuberculosis of the lungs. A definite diagnosis can be made only after carefully observing the case for some time, and in many instances is reached only at necropsy. Latent exophthalmic goitre, with tachycardia, very slight exophthalmos, some fever, pronounced weakness, and a marked cardiorespiratory murmur offers considerable difficulty. Resort at times must be had to tuberculin.

Syphilis of the lung may closely resemble tuberculosis, and the diagnosis rests in many cases upon the history, other luetic lesions if present, the results of antiluetic treatment, and the absence of tubercle bacilli. The root of the lung is found more often involved, while the apex escapes. Destructive or diffuse sclerotic changes may occur in syphilis. Cases occur with slight fever and slight or indefinite pulmonary symptoms. Tuberculin may be used.

Bronchiectasis may so closely simulate tuberculosis that repeated sputum examinations may be necessary to decide the question. Dulness is more apt to be lacking in bronchiectasis, and the base and posterior are more often affected. When bronchiectasis occurs at the apex the diagnosis is difficult. The history may be important. Early hæmoptysis favors tuberculosis, while copious expectoration in paroxysms, which is at times fetid, and without tubercle bacilli or elastic fibers, bespeaks bronchiectasis. It is not uncommon to have bronchiectasis in old tuberculous lesions.

In pulmonary gangrene the large quantity of sputum coughed up at one time, its foul odor, its separation into layers, and the absence of tubercle bacilli, as well as the location of the lesion, usually basal, determine the diagnosis.

Some cases of pleurisy with effusion so closely simulate pulmonary tuberculosis that experts have been deceived. The whole of one side may be affected and shrunken. Dulness is more or less marked, resistance increased, and auscultation reveals a distant respiratory murmur, possibly bronchial in character, with pleuritic friction sounds or numerous moderately coarse mucous rales widely heard over the side. The symptoms may be indistinguishable from those of phthisis. Tubercle bacilli are absent from the sputum, and the aspirating needle reveals a thick fluid, perchance with many cholesterin crystals, or possibly a little pus if infection has taken place. Signs of cavity may be present.

The parasitic diseases of the lung most often confused with pulmonary tuberculosis are those caused by the lung fluke (*Distomum pulmonare*) and hydatids. The former disease is quite frequent in parts of Japan and is consistent with years of active life. The most important symptom of this disease is hæmoptysis. The discovery of the eggs in the sputum or

blood will confirm the diagnosis. In hydatid disease of the lung the presence of the wall membrane or of hooklets in the sputum is pathognomonic. The distribution of dulness may be unusual and excite suspicion. The respiratory murmur and vocal fremitus may be absent. The upper lobe is usually involved.

Actinomycosis is at times readily diagnosed from the sputum. It frequently attacks the chest wall. In anthrax the bacilli are found.

*Streptothrix pseudotuberculosa* (Flexner), *Cladothrix asteroids* (Eppinger), protozoan infection (Rixford and Gilchrist), and *Aspergillus fumigatus* (Renon) can all produce the same symptoms and physical signs as pulmonary tuberculosis. A careful examination of the sputum in some cases aids greatly in diagnosis.

Tumor of the lung more often simulates pleurisy with effusion than pulmonary tuberculosis, but at times it closely resembles a massive tuberculous consolidation. The abnormal position of the heart and the usual absence of fever are important points in separating it from tuberculous disease. Dyspnœa, fever, and emaciation may be combined in cancer, but it is of rare occurrence. Involvement of the glands may be of late occurrence in malignant growths. The sputum may resemble raspberry or currant jelly.

Slight valvular insufficiency in chronic heart diseases may produce bloody sputum and, if infarct occurs, some temporary fever, pain in the side (pleurisy), rales, and possibly bronchial breathing. In some cases mitral stenosis has been regarded as pulmonary tuberculosis.

## PROGNOSIS.

**The Basis for Scientific Prognosis.**—Prognosis in the final analysis depends upon the number and the virulence of the infecting bacilli and upon the resistance of the patient, two factors about which our knowledge is most indefinite in any individual case. Furthermore, their influence cannot be separated one from another. The number of the infecting organisms can never be determined, but the virulence may be roughly estimated by animal inoculation. The resistance of the patient may be indicated by a limited lesion (resistance to the bacillus) or by slight symptoms (resistance to the toxin) even when the symptoms (fever, tachycardia, emaciation, etc.) are severe, or the signs very extensive. A double resistance is of course most favorable, and a resistance to toxin is, on the whole, more favorable than a resistance to the bacillus, or it may be the latter is more easily acquired or more generally possessed than the former. There is a well-marked tendency to recovery in pulmonary tuberculosis, as postmortem statistics show. Most authorities have noticed that in a few patients in an advanced stage the disease shows a self-limitation and intrinsic tendency to recovery. Prognosis can be discussed in regard (1) to the danger to life, (2) to the curability, and (3) to the course and duration.

The marked tendency to *relapse* (following the false convalescence of Laennec), so often present, is unfavorable, although relapse after some years of good health, during which the patient has led an ordinary life, is only slightly less favorable in regard to prognosis than a primary attack. Relapse under favorable conditions is always more serious than under adverse circumstances, either in regard to work, hygienic or climatic conditions,

Nowhere in medicine can it be said more truly that experience is fallacious and judgment difficult than in regard to prognosis in pulmonary tuberculosis. A limited experience often leads one to risk a positive prognosis, but with further knowledge and the recollection of numerous mistakes comes the humility of uncertainty. He is wisest who says least. It is better in all cases to defer a prognosis until the patient has been observed for at least a month or until it can be seen how he responds to treatment. Gee has well said that he who would foretell when a consumptive will die can be sure of but one thing, that he will be mistaken. "In a disease where the unexpected so often happens, where the casual and unforeseen play so large a part, where the patient's wisdom, courage, and self-control count for so much, the prognosis should always be guarded, and a dogmatic attitude avoided" (Lindsay).

**Age.**—After the fourth semidecade of life, the prognosis with each year becomes less favorable, and after the forty-fifth year it is not good for curability, but the disease can usually be arrested or, if progressive, runs a slow course. Before the tenth or twelfth year lack of self-restraint would seem to, but does not, render the ultimate prognosis unfavorable. Acute tuberculosis is more frequent in younger patients, but the prognosis in the chronic types is, *cæteris paribus*, at least as favorable as in later years. Flick and Turban think the prognosis more favorable in children, and West and Cornet believe a rapid course is more likely in young adults and elderly persons. Many hold that prognosis is worse between the ages of fifteen and twenty-one years, but adduce for the most part only "personal experience," the cloak for inexact clinical observation.

**Sex.**—This, *per se*, seems to exert little influence. Just as the closer confinement to which women are subjected renders them more susceptible, so the ties and household duties, which can be less easily avoided than the occupations of the males, have a more serious effect. Marriage complicates the prognosis much more in women than in men, but under certain conditions may aggravate the prognosis in either sex. Puberty and the menopause are considered by some to have an unfavorable influence. Widowhood is serious for both sexes. The rough, exposed life at times incident in the treatment of pulmonary tuberculosis is more suitable to males. However, pregnancy may be considered the most important factor in regard to sex. Women with marked menstrual disturbances are less likely to do well.

**Heredity.**—The individual susceptibility is held by many to be inherited. It is believed to come from forebears weakened from any form of disease, not necessarily tuberculosis. However it may be, certain families show a predilection to an acute course, others to a chronic course and recovery, and some, it is held, are more susceptible to certain complications (laryngitis). In general, heredity seems to play a far less important part in prognosis than was formerly thought, and the general opinion today is that, once infected, heredity has little further bearing upon the case. Heredity might often read house infection (Lindsay). In fact, Reibmayr and later King believe that children of tuberculous parents and grandparents have increased resistance to tuberculosis. Children of old fathers, the younger children of large families, children of parents (especially the mother) weakened at the time of conception or pregnancy, all may have lessened resistance.

**Environment.**—The present and future environment of any patient is far more important than the former surroundings. The latter, however, are

not without influence, though this may be in part due to the bearing the former has upon the present or future occupation. Patients (males) with outdoor occupations do less well during sanatorium residence than those who have worked indoors. Patients from the country do not do as well as those from the city. The explanation no doubt lies in the greater change. Pulmonary tuberculosis contracted under bad environment is much more likely to do well, when the surroundings are changed than when the disease occurs with good surroundings. Further, the working classes, especially those who do manual labor, are likely to do much better if a "cure" has been effected at home, for in this case a suitable future environment is assured, which is not the case when the patient returns from a sojourn in a health resort to poor hygienic conditions and hard manual labor in order to support a large family.

Patients who find light employment without too much responsibility in suitable climates or in the country will do better. Close confinement in the larger cities is always a serious matter. Patients who return to a nagging wife or family should receive a doubtful prognosis. The fact that some member of the family has visited them during their sojourn at the health resort greatly increases the chances of permanent recovery, for the family, too, then knows what should be done. In other words, the more nearly the future environment can approximate that under which the "cure" has been effected, the better the prognosis. For this reason, patients who after recovery continue to live in good climates have a better prognosis than those who return to their former homes. Patients with ample means should, therefore, receive a better prognosis, but only if they fully realize that money is but an adjuvant, not a true means, to recovery. For all these reasons environment is probably the most essential factor in prognosis after arrest is once established.

**Character and Disposition.**—The habits are of great importance, and a methodical individual, not too lethargic, has always a more favorable prognosis. A former immoral, dissolute life indicates usually a harder struggle, but the prognosis is worse in those patients who have always followed only their own bent, irrespective of the wishes of others. Patients with a love of nature, of birds and flowers, do better than those whose hobbies keep them indoors.

A bright, cheerful disposition betokens a better prognosis than a moody, morose, and taciturn temperament. But a patient who is too sanguine, who has really nothing the matter with him, who is so hopeful that details of treatment will be passed by, is not to be looked upon too favorably. Vacillation, lack of self-control, stubbornness, and lack of imagination or foresight are all unfavorable. Patients who need constant watching, who rely upon the physician for every detail of their life, lose the power of self-control, of self-reliance, and are often led, when out of their physicians' influence, to do foolish acts. Such deserve a doubtful prognosis. The degree of intelligence is important. "I am impressed," writes Flint, "with the force of this statement, namely, most patients who recover from phthisis are persons of resolution and perseverance; persons who appreciate the nature of the disease and are determined to overcome it. The disease, as is well known, is apt to induce either delusions concerning danger or a state of passive acquiescence therein. The will may become here, as in some other diseases, an efficient agent in promoting recovery, and it is therefore an important

element in prognosis. So far as the mind is concerned, the most favorable condition is that in which the patient appreciates fully the situation and is resolved to spare no efforts in becoming master of it, having much faith in his ability to succeed." Patients who have never been ill or who have always recovered rapidly from illnesses deserve more favorable prognosis. A previous susceptibility to catarrh and colds is unfavorable.

**Mode of Onset.**—A sudden onset is usually more favorable in that the patient consults the physician at once and does not wait until the disease is far advanced and symptoms pronounced. This is no doubt the explanation of the favorable course of many cases with an onset with hæmoptysis or pleurisy, for the percentage of favorable results stands in inverse proportion to the duration of the disease as well as to its extent (Turban). Patients with an insidious onset or even the catarrhal form may for the same reason present a more serious picture, although in itself the onset affords little aid in prognosis. The pneumonic, gastric, or laryngeal onsets offer usually a worse prognosis. A glandular onset generally betokens a chronic but often a fatal course. An acute onset with extensive or marked physical signs is the most unfavorable, but the onset may be acute and the patient rapidly recover. An onset consecutive to some debilitating disease, *e. g.*, typhoid fever or measles, is often unfavorable. A pleuritic onset, a slight friction rub here and there, with slight symptoms and few other signs, are considered by Osler favorable, by Maguire most unfavorable. The mode of onset is connected with prognosis, chiefly in its bearing upon the diagnosis.

**Weight.**—This is of much prognostic significance. Loss of weight at first is almost universal and if this approximates one-quarter of the body weight it is of grave import; if it reaches one-third, a fatal outcome is almost certain (Chaussat). A gain in weight under forced feeding is of less hopeful significance than a gain on an ordinary diet, but a rapid gain of some pounds is of vastly less moment than a steady but even smaller gain extending over a long period. Too much importance must not be attached to the twenty or thirty pounds gained by patients in advanced stages under the influence of climatic change and good food. A steady loss of weight is more unfavorable than continuous pyrexia, and if both continue when the patient is put under the proper treatment the outlook is particularly dark (A. Fränkel). In a few cases patients, often chlorotic, go steadily down hill, but lose little or no weight. Œdema may mask loss of weight. The disease in a patient who has always been markedly under weight (twenty to twenty-five pounds) usually runs an unfavorable course, although numerous exceptions occur.

The digestion is the keystone in the prognostic arch. If it fails, the outlook is indeed gloomy. As long as it remains good and the patient can take sufficient nourishment there is hope. Patients who always have had a poor appetite, who have eaten little, usually have an unfavorable course (Brehmer). Persistent anorexia is very unfavorable. Strong antipathies to the proper food, *e. g.*, milk, eggs, meat, is also of evil omen. Indigestion, if chronic and severe, clouds the prognosis. Patients with gastric ulcer often do remarkably well. Marked cachexia is always grave and usually indicates severe chronic tuberculous intoxication. The preservation of the teeth, Ferrier believes, is a sign of spontaneous curability, as it indicates absence of decalcification. It is more important in its bearing upon the digestion.

**Fever.**—Elevation of temperature is one of the most accurate indications of activity in the pulmonary lesion and for this reason is of vast importance.

With apyrexia the local lesion rarely makes much progress (Osler). A temperature curve whose minimum never falls to normal indicates progressive disease better than any other signs. Continuous high pyrexia with marked remissions (as low as 93° to 97°) is usually indicative of septic absorption, cavity formation, and far-advanced disease, with little hope for permanent improvement. Subnormal oral temperature, if the circulation be good, is of no prognostic significance (especially in winter). Daremberg believes, however, that patients with an oral temperature below 97° have less chance of improvement than those whose temperature never falls below 98°. Low temperatures are most serious when they occur between 7 A.M. and midnight. Marked fever with slight physical signs, if of any duration, is always of serious moment. The inverse type of temperature curve, *i. e.*, highest in the morning, usually indicates a higher temperature during the night, and is a most unfavorable sign. Persistent fever under suitable treatment is far more unfavorable than recurrent fever which quickly responds to treatment, but frequent attacks of pyrexia cloud the prognosis. As long as the nutrition is good there is hope of the fever subsiding. The prognosis is also governed by the time the fever has lasted, and even slight fever (99.6° to 100°) when persistent is ominous. The height of the fever is not of itself a bad sign (Schroeder). Collapse temperatures usually indicate approaching death. Absence of fever may mean immunity to the toxin or lack of resistance.

**Circulation.**—The pulse in the majority is the best prognostic sign, and together with the temperature and weight might be termed the prognostic triad. It is the most sensitive of the three, and the most easily affected by external conditions. A continuously fast pulse, when noted not only in the office but at home, indicates a poor prognosis. The pulse in the office is nearly always quickened and affords little data for prognosis. Further, it must not be forgotten that the temperature almost invariably reaches normal before the pulse. A slow pulse with an elevated temperature indicates fever of recent origin or a favorable prognosis. A pulse constantly above 100 during rest is always serious, but a few patients, fully recovered, suffer for years from tachycardia. A pulse out of proportion to the fever indicates that the disease will advance in spite of the low temperature (Sirot). Arthaud believes a pulse constantly above 110 indicates a fatal ending. Schneider, who considers 90 the normal pulse in pulmonary tuberculosis, followed 1000 patients discharged from the Weicker Sanatorium for four years. In the first stage (Turban) 80 per cent. of those alive had had a normal pulse, and 97 per cent. of those dead a rapid pulse; in the second and third stages the figures were 81 per cent. and 81 per cent., and 73 per cent. and 79 per cent., respectively. Advanced cases with a normal pulse he found did better than incipient cases with a rapid pulse. Undue irritation of the pulse (heart) is unfavorable. A study of 510 cases at the Adirondack Cottage Sanitarium upholds these statements.

Cyanosis of the lips, face, and extremities usually occurs only in desperate cases, but many patients with slight cyanosis, especially of the nails, may live for years and enjoy a fairly active life. Cyanosis following hæmoptysis, especially if accompanied with tachycardia and dyspnœa, is of most serious moment and death usually occurs shortly.

The arterial tension has not been shown to have any great significance in prognosis. Arteriosclerosis is unfavorable. Marked accentuation of the second pulmonic sound is unfavorable in Flick's opinion, but some

others hold that it indicates a strong and probably hypertrophied right ventricle, and is, therefore, favorable. Disappearance of this accentuation with increasing dyspnœa and tachycardia indicates a failing right ventricle and may precede dilatation, but without dyspnœa and with a good pulse it indicates an improved circulation and a favorable prognosis. In pulmonary tuberculosis associated with heart disease, the prognosis is that of the more pronounced disease. Patients with mitral disease do better than those with aortic disease. If compensation be good and the pulmonary tuberculosis slight, prognosis for life is good. Acquired dextrocardia is indicative of chronicity and is not in itself unfavorable.

**Hæmoptysis.**—This may occur as an accident in the course or as a symptom of an advancing process. The prognosis is very different, and when unaccompanied by fever, rapid pulse, shortness of breath, or cyanosis, hæmoptysis is often of little moment. The so-called "hemorrhage cases," which are supposed by many to do better than others, have as a rule a slightly less favorable prognosis. Hæmoptysis is always more likely to recur in such patients than in those previously free from it, and the danger of aspiration pneumonia or dissemination is always present. This danger is greatly increased in nervous, excitable patients. As a rule, hæmoptysis is rare in acute cases. In advanced stages with cavity formation hæmoptysis is always serious, but an absolutely hopeless prognosis should never be given. Sudden death, except from hæmoptysis, is rare in pulmonary tuberculosis. Recurrent hæmoptysis at the menstrual period may eventually terminate in death.

**Nervous Symptoms.**—In prognosis the nervous system is second in importance only to the digestive and circulatory systems. In all patients in whom the nervous, neurasthenic, vasomotor, trophoneurotic or nervous-dyspeptic symptoms are pronounced the prognosis is bad. The so-called erethistic group belongs in this class. A few hysterical patients do remarkably well. In the mentally deficient, or even in those of a low grade of intelligence, the outlook is more serious.

**Amenorrhœa.**—Amenorrhœa indicates in most cases advanced disease, and is, therefore, of serious import when continued over long periods. Return of menstruation is favorable, but little conclusion can be drawn from a continuance of this function, as it may persist to the end.

**Cough.**—The improvement of cough if gradual and continuous is favorable, for in its indirect effects severe cough that cannot be checked is most serious.

**Respiration.**—The rate helps little until late in the disease, when other signs tell of the downward course. Marked disturbance of the pulse-respiration ratio is unfavorable.

**Urine.**—*Albuminuria* from any cause, if more than transient, is of serious moment. Tuberculous nephritis, if confined to one kidney, which receives proper treatment, may be recovered from, but greatly increases the danger. Prognosis is more favorable when the amount of nitrogen excreted in the urine is large (Mircoli). A gradual diminution of the solid matter in the urine without increase of weight is of unfavorable import (Robin).

**Diazo Reaction.**—The *diazo reaction* is recognized to have marked limitations in regard to prognosis. On the whole, however, if the patient has no kidney affection, has taken no salol or other drug which affects it, the constant occurrence of the diazo reaction may be considered as an unfavorable sign. The intensity of the reaction is of considerable importance. It is

usually connected with fever, and occurs in some cases during the tuberculin reaction.

Ehrlich's dimethylamidobenzaldehyde reaction has no prognostic value. The phosphatic or calcium content, the albumose, and the hyperacidity are of little value.

**Blood.**—This affords singularly little basis for prognosis. Increase of hæmoglobin and of erythrocytes is usually favorable. In advanced cases a decrease of the leukocytes is unfavorable; an increase of the lymphocytes and transitional cells is possibly favorable. Arneth's work upon the polynuclear leukocytes may prove to be of value. An increase of cells with fewer nuclei is held to be unfavorable, an increase of those with many nuclei of favorable import. The eosinophiles are of little value in prognosis (Ullom and Craig). Quinquad believes that if the glycogen in the blood of a patient falls below 0.16 gr. per 1000 a speedy death is certain. The agglutination phenomenon affords only too little practical help in prognosis, but Wright's opsonic index method may prove in time to be of value.

The general constitution of the patient is of less importance than would be supposed. Acute types often occur in robust individuals; great muscular strength in a patient with pulmonary tuberculosis demands a careful prognosis on account of the tendency to overdo, to overexert, and so cause hæmoptysis. On the whole, a good constitution demands a more favorable prognosis than the opposite, although some large, well-nourished individuals give the impression of being "soft" and lacking resistance, while other wiry, thin, flat-chested individuals do remarkably well. Florid subjects are less favorable. Individuals with red or fair hair do better than those with dark or black hair (Shrubsall).

The *habitus phthisicus* of itself is not always an unfavorable sign, but fewer patients with such bodily conformity make a good recovery. The shape of the chest yields little or no information (on the whole) for prognosis, when it departs but slightly from normal (*e. g.*, mild, rickety chest). A paralytic or deformed thorax which limits respiratory movement is unfavorable.

**Physical Signs.**—Physical signs tell what injury has occurred in the lungs, the constitutional symptoms what is occurring at present, and only by a careful consideration of both symptoms and signs can we hope to arrive at an approximately correct prognosis. Physical signs yield little or no evidence in regard to activity or arrest in the pulmonary process and only by carefully noted and repeated examinations can much stress be laid upon them in prognosis. The signs of softening for instance are notoriously uncertain. For these reasons physical signs are for prognosis of far less importance than symptoms. The physical signs indicate not the amount of poisoning, but the amount of local reaction of the tissues.

The *site* of the lesion is not unimportant. Unquestionably the disease is discovered earlier at the apex, and for this reason, if for no other, the prognosis is usually more favorable. Primary infections of the base are generally held to be due to an overwhelming dose of the infectious material and so are of grave significance. Maguire, however, believes a primary basic lesion is rare, but very favorable if not grafted upon a pneumonia, while a lesion beginning in the middle lobe is always bad. There is no difference in gravity between the right and left side, although in some instances, through loss of covering or displacement, the heart is more irritable when the left lung is affected.

Physical signs, unless consolidation be present, tell unfortunately little of the extent of the lesion in the third dimension (depth). A large portion of the interior of the lung cannot be examined except by *x*-rays, which in some instances yield information most important for prognosis. *Cæteris paribus*, the prognosis, more especially in regard to cure, depends directly upon the extent of the lesion. The fact, however, that an accompanying acute non-tuberculous bronchitis in the smaller bronchial tubes may greatly increase the "extent of the lesion" temporarily should be borne in mind. Notwithstanding this, Turban and Rumpf believe extent of the disease outweighs all other factors in prognosis. As long as the disease is confined to one side the prognosis is better, but slight involvement of both apices is frequent in most favorable cases. Physical signs at an apex and base posteriorly are thought by Fowler to be produced by tuberculous and non-tuberculous disease respectively, and such cases are held to be much more favorable than those with even slighter physical signs which extend from apex to base, and which are produced by tuberculosis. In a number of patients moderately coarse rales, rather superficial, can be detected after coughing over the whole of one or possibly both sides. These may be the only physical signs and the patient may be without symptoms. The prognosis in such cases is favorable for arrest as long as great care is exercised. Widely extended pleurisy runs a favorable course (Osler). Scattered foci, even though scarcely perceptible, are always of bad omen, but it is never safe to give an absolutely bad prognosis on physical signs alone. The extent of the lesion in relation to the duration of the disease and the severity of the symptoms is of great importance in prognosis. A limited lesion with disease of some duration is always favorable, while an extensive lesion of short duration demands a bad prognosis. Whenever the extent of the physical signs and the symptoms are disproportionate, *i. e.*, when severe symptoms occur with slight physical signs, the prognosis is grave. The mere fact that no definite line of march can be made out is often in itself of the greatest importance, as it may indicate that the disease will run a rapid course (Fowler).

A limited lesion, even in a more advanced stage, is more favorable than one of wide extent. A sharply defined cavity at one apex is more favorable for duration of life than an infiltration scattered over one to two lobes, but the majority of patients with arrest show only signs of infiltration. The larger the cavity the greater the risk of profuse hæmoptysis. Excessive fibrosis in both lungs is unfavorable. Leathery, creaking sounds replacing the mucous rales are often the first indication of subsidence of the acute process. Slight changes in percussion and breathing without rales are the most favorable physical signs. The finer the rales the better the prognosis. Rales at an apex may persist long after all symptoms have disappeared and too much importance should not be attached to them. A complete and constant absence of all rales after coughing is very favorable.

The condition of the unaffected or less affected side must always be carefully determined. Unilateral disease, with shrinking, is always more favorable if accompanied by compensatory hypertrophy of the opposite lung.

A point of special interest is the fact that a patient will often become afebrile, have a lower or normal pulse, less cough and expectoration, gain weight, and in every way indicate that he is improving, and still on examination the physical signs be found more pronounced or scattered over a wider area. The most probable explanation of this fact is that the disease

was present in the whole area at the first examination, but the organism was not able to react to its stimulus. As the patient gained strength, the tissues "reacted" and the physical signs increased while the patient improved. The intensity of the lesion is less important than the extent. A sharp demarcation betokens a favorable course.

**Sputum.**—A gradual change from a purulent to a mucoid sputum is favorable. A sudden change from a purulent to a frothy, watery sputum is of bad omen and often indicates the onset of miliary or acute tuberculosis. When mucoid sputum becomes mucopurulent or purulent an acute process should be suspected, and if it contain elastic fibers and numerous tubercle bacilli where before there were few or none, a more or less extensive softening is present, and if coupled with other symptoms, a doubtful or bad prognosis should be given. Lung stones occur nearly always in unfavorable chronic cases. Aspiration is more likely to occur when the sputum is thin and watery than when it is thick and mucoid.

A gradual decrease in the amount of sputum is favorable; a sudden decrease may indicate heart failure, a congestive process, or possibly acute miliary tuberculosis. The absence of sputum is not necessarily a favorable sign. Large amounts of sputum daily for any length of time usually indicate extensive bronchial irritation and are unfavorable. A bronchorrhœa, however, may persist for months and the patient do well.

*Tubercle Bacilli.*—The occurrence of tubercle bacilli in the sputum always indicates ulceration and such patients have accordingly a less favorable prognosis. Rumpf believes a patient in the third stage (Turban) without tubercle bacilli deserves a better prognosis than a patient in the second or even the first stage with tubercle bacilli. The longer tubercle bacilli occur in the sputum the less favorable the prognosis, although some patients can have tubercle bacilli for years in the sputum and do well or, indeed, even finally recover.

The unequal distribution and the possible variation in staining of the bacilli, the temporary occlusion of the focus, the fact that patients with rapidly advancing disease may give off few bacilli and fully encapsulated cavities in arrested patients, enormous masses, visible when stained to the naked eye, all emphasize great caution in prognosis from the number of bacilli. From one specimen nothing can be told, but if in a series of examinations at sufficiently long intervals the number of bacilli steadily decreases, the prognosis is more favorable than if the number remains stationary or increases. A sudden increase in tubercle bacilli, which before were very scarce or absent, indicates usually rapid softening. An early disappearance and persistent absence of tubercle bacilli during treatment is most favorable.

The distribution of the tubercle bacilli in clumps usually indicates a severe type of disease. Loose clumps occur more often in unfavorable cases. Chains of three or more bacilli and pairs or clumps of parallel bacilli give no data for prognosis. Enormous masses of bacilli may occur in very favorable cases.

Morphology affords little aid, but short bacilli are suggestive of a more active process, more long and short bacilli and fewer medium occur in the most unfavorable cases, where also irregular and beaded bacilli are most frequent. Short bacilli are usually held to indicate an active growth of the infecting organism, and so an unfavorable prognosis. According to

most observers, however, long, slender, beaded, irregular bacilli indicate a chronic course, but not necessarily a favorable termination. The same is probably true of the bacillary fragments, "splitter."

*Secondary infection* is *a priori* unfavorable, but owing to the great difficulty in diagnosis cannot be relied upon for prognosis. The danger of secondary infection is chiefly the occurrence of pneumonic processes.

The phagocytic power of the cells in the sputum for tubercle bacilli has been found by Allen, of Saranac Lake, to be of slight if any value for prognosis, but Loewenstein on rather few observations concluded that it occurs in early pulmonary tuberculosis which tended toward healing and in chronic types. Elastic fibers are now seldom found in sanatorium patients and their constant presence is of very unfavorable import. Fibrinous coagula (fibrinous bronchitis) are of bad prognostic omen.

**Complications.**—The occurrence of any complication is of unfavorable moment, but all of a tuberculous nature bespeak a lessened resistance and are accordingly of grave prognostic significance. Simple acute or even chronic *laryngitis* is of slight importance, but tuberculous laryngitis makes the prognosis at once grave. Slight ulceration of the cords without infiltration is the least unfavorable form. When complicated with dysphagia the condition is most serious. Simple acute *bronchitis*, especially if the attacks are frequent, clouds the prognosis. In advanced stages it may be the primary cause of death. *Acute lobar pneumonia* is always serious and often results in death in advanced stages.

Dry *pleurisy* as a complication, even if extensive, is not unfavorable. The effect of a pleuritic effusion depends partly upon the size of the effusion, partly upon the stage of the disease. Louis, Walshe, and West held that effusion exerts an unfavorable influence, Flint that it is without influence, and some hold (Murphy) it may by compressing the lung favor healing. As an onset it is distinctly favorable; during the course it exerts little influence. Hemorrhagic effusion is always serious. Empyema is rarely recovered from. *Pneumothorax* is always most serious and recovery is of the rarest occurrence. Death inside of one month is the rule, but the majority die in a few days. The condition of the opposite lung is of extreme importance in prognosis.

Non-tuberculous *enteritis* seems to be well borne, especially if of the neurotic type. Tuberculous enteritis occurs usually late in pulmonary tuberculosis, when the fatal termination is not far distant, but recovery can take place. Lardaceous disease which may produce diarrhœa precludes recovery.

Arthritis, rheumatism, mitral stenosis, cardiac hypertrophy, slight emphysema, bronchial asthma, and gout have all been held to exert a favorable influence on the pulmonary tuberculosis. Typhoid fever is not necessarily unfavorable. Diabetes mellitus, pulmonary stenosis, pulmonary gangrene, lardaceous disease, tuberculous stomatitis or pharyngitis, severe thrush, meningitis, œdema, melancholia, insanity are always of very grave if not fatal prognostic significance. Mild diphtheria exerts but little influence when properly treated. Syphilis is said in the early stages to be unfavorable, but is certainly well borne in many patients who ultimately recover. Bronchiectasis is unfavorable. Enlargement of the thyroid is not unfavorable unless accompanied by symptoms. Tuberculous otitis media and slightly enlarged lymph glands occur in patients whose disease runs often

a chronic and possibly an unfavorable course. Persistent anæmia is unfavorable. Fistula-in-ano exerts little influence and is not unfavorable. Chronic peritonitis, even if pelvic, is unfavorable.

The duration of treatment is important. Little can be expected from a cure of less than three months, and the best results are those obtained after three or four years.

Prognosis is always uncertain. The anamnesis is of less value than the actual condition. Symptoms are of more value than physical signs, and are, in the order of their importance, those referable to the digestive tract (including weight), to the nervous system (including character), the pulse rate, and the fever. Complications, especially if tuberculous, are always to be dreaded. The urine, the sputum, and the blood are of far less value in prognosis than the foregoing. Race, age, sex, heredity, mode of onset, the shape of the chest, spirometry, etc., are of only secondary importance, and, like the urine and sputum, helpful if they concur with the symptoms and physical signs, of little value if they contradict them. The financial condition and the environment of the patient should always be considered.

# CHAPTER XI.

## THE PROPHYLAXIS AND TREATMENT OF TUBERCULOSIS.

By LAWRASON BROWN, M.D.

### PROPHYLAXIS.

**Historical.**—From time to time it is valuable to pause in order to review the methods employed and the results that have been obtained in any work. Since 1882 it has been known that tuberculosis is due to a microörganism, but Villemin, in 1865, had already shown that it was infectious. Nevertheless, it is only during the last decade that the antituberculosis struggle has begun in earnest. One country, England, has long shown a decreasing death rate from this disease (from 247 per 100,000 in 1851 to 136 in 1900), and inquiry shows that it is in all probability due mainly to the fact that hospitals for patients in far-advanced stages and infirmaries in connection with poor-houses (Newsholme) were long ago established and that the improved sanitation and general hygiene have greatly raised the resistance of the individual. The tubercle bacillus was unknown when England's mortality began to lessen markedly, and no provision was taken against infection. The results in Germany have been particularly gratifying and the mortality reduced from 357.7 per 100,000 in 1877 to 1881 to 218.7 in 1897 to 1901 and 190 in 1902. The crusade in France has been based upon the struggle against predisposition. They have clearly grasped the fundamental fact that the children must be cared for, and were the first to develop the sea-side sanatoriums for children, although the first sea-side hospital was founded in England in 1796, at Margate.

The struggle in Denmark has centred around the excellent work of Bang, who has shown that, by the use of tuberculin and isolation, cattle tuberculosis can be exterminated. Norway has drawn upon its experience with leprosy to put in practice some of the procedures used to exterminate that scourge. Compulsory notification and removal when necessary to suitable sanatoriums and hospitals are now in force, and the results are satisfactory. To Spain (Valencia, 1689), to France (Nancy, 1750), and to Italy (Naples, 1789) belong the honor of passing the first laws dealing with pulmonary tuberculosis. They ordered the burning of all linen, bedding, and beds, but metal objects were exempted. It remained, however, for America to organize, first, the modern municipal struggle against tuberculosis. Too great honor cannot be paid to Biggs, of New York, who almost single-handed forced upon that city what are now recognized as the most efficient prophylactic measures against tuberculosis. To Biggs and to Flick, who standing alone forced upon an undivided doubting medical profession (of Philadelphia) his views of house infection, America owes most in prophylaxis. More recently Koch has denied any great danger of infection from milk, while v. Behring attributes to this food the chief danger which he says occurs in

childhood. That tuberculous infection takes place most often through the sputum can safely be affirmed, as well as the fact that some danger, however great or small it may be, lurks in milk of tuberculous cows.

Prophylaxis can be reduced to two fundamental factors, destruction of the specific germ and increase in the individual resistance. The chief source of tubercle bacilli in the air is the sputum, dried and ground into dust or (of less importance) sprayed into the air in coughing. The tubercle bacillus is not ubiquitous, and is usually found only near the tuberculous patient. The individual resistance is probably what has enabled any individual of middle age to escape serious infection. The struggle to raise the resistance begins at birth and continues through life. The crusade must be against tuberculosis and not against the tuberculous patient.

**State and Municipal.**—Prophylactic measures can never be as immediately efficient as similar measures against other infectious diseases. The majority of instances of acute infectious diseases are in children; the number of individuals attacked at one time in a community is limited; the date of onset and of full recovery can be closely approximated; the infectious period is short and coincides in part at least with restricted movement due to disability, and the economical loss is slight. In tuberculosis, young adults are chiefly attacked, the onset is frequently overlooked, the number of individuals attacked at one time is much larger, the movement is little restricted for months or years, as the disability is often slight while the infectiousness is great, and the economical loss enormous. So many and varied etiological factors enter into infection in tuberculosis, and so many of these are so closely bound up in the individual relations, that it will never be possible to legislate against tuberculosis as against smallpox or plague. Much, however, has and can be accomplished by intelligent legislation. Prophylactic laws should be passed governing the army and navy, the restriction of animal tuberculosis, and the sale of tuberculous milk and meat. The notification of tuberculosis; the regulation of trades, workshops, and traffic; the construction of houses, including tenements; a campaign of education, and the erection of special hospitals, dispensaries, and sanatoriums should be carefully dealt with.

**Army.**—The question of prophylaxis is one of importance, especially for all countries where military service is compulsory. The recent work of Franz, who found that 60 per cent. of the young recruits of an Austrian regiment reacted to tuberculin, clearly proves this. As the majority of cases in the army occur in the first six months of service (Kelsch), prophylactic efforts should be redoubled during this period. Individuals formerly tuberculous should be exempt from military service and all recruits with a suspicious history should receive a careful and thorough examination. Such recruits, especially if a history of a previous attack of pleurisy or an exposure to infection has been obtained, should for a time be drilled apart and less rigorously. Repeated examinations of the chest and sputum should be made. Barracks should be properly constructed, periodically disinfected, and all rules of individual hygiene, especially those about promiscuous expectoration, strictly enforced. The army should have its own sanatorium, where patients should be sent at once.

**Navy.**—The confined quarters, almost of necessity overcrowded and ill-ventilated, even of the battle-ships today, render the men more susceptible. The greatest care should be exercised in the preliminary examinations,

especially before long cruises, and about sputum disposal. The smaller craft, plying along the coast, should be carefully inspected and placarded, and notification of pulmonary tuberculosis should be insisted upon, in order to carry out disinfection.

**Regulations against Animal Tuberculosis.**—Convincing proof has been adduced that the human and bovine diseases are intercommunicable; and even if the facts that are slowly accumulating show that infection with the bovine tubercle bacillus occurs infrequently, it should, nevertheless, be vigorously combated. In Koch's opinion the danger from hereditary transmission and from milk and its products are about equal.

*Dairies.*—Model dairies have been started in many States and countries, and Coit, of New Jersey, has patented the term "certified" to ensure that all dairies using it dispense milk approved in regard to purity and quality by a medical committee of the community. The value of these provisions in the prophylaxis of pulmonary tuberculosis is apparent. All cows must be tested with tuberculin before admission to such byres, and after admission retested at intervals. The stables must be open at all times for inspection by the proper authorities. While it may not be possible for all municipalities to adopt such stringent supervision of all dairies supplying milk, still each city should have its Milk Commission, whose duty should be to inspect and to license all dairies.

Milk from tuberculous cows with healthy udders has been found infectious by Ernst, Mohler, and Rabinowitsch, though Adami questions the virulence of such bacilli. Such milk has been considered safe after boiling, but Smith has pointed out that boiling even for ten minutes is sufficient only if no pellicle forms upon the surface, and Calmette and Breton have recently asserted that dead tubercle bacilli in such milk are injurious and affect healthy guinea-pigs like small, repeated doses of tuberculin. Von Behring is much opposed to Pasteurization or boiling of milk, as he claims that it alters the immunizing qualities of the milk from immunized cows. In Denmark all butter for export is prepared from cream, heated to 80° to 85° C. All milk from an uninspected dairy should be boiled or heated in this way, especially if used by children, invalids, or convalescents. Properly boiled in a double kettle (boiler), with a rather close-fitting cover and cooled at once without uncovering, the taste is said to be unchanged.

Tuberculous cows should always be isolated, not housed; and it is wiser to use them only for breeding or working purposes, removing the calves at birth, as only one-third of 1 per cent. are tuberculous at birth (Bang). Cows with tuberculous mastitis, metritis, or enteritis should be killed. From 1 to 10 per cent. of tuberculous cows have mastitis. Cattle once reacting to tuberculin should be branded. Repeated injections may produce a tolerance, a fact made use of by unscrupulous dealers. Cattle which have been on a journey generally react but slightly for some time, due probably to the inhibiting effect of mental excitement on the heat centre (Bang).

The method of vaccination with living bacilli is now being widely tried, apparently with great success, especially by Pearson and Gilliland, in America. Von Behring also advocates passive immunization of calves by the use of milk of immunized cows. Immunized calves should be fed on milk from cows free from tuberculosis.

*Slaughter-houses.*—Tuberculous meat is of far less importance than tuberculous milk. The danger of such meat lies in the fact that the centre of a

"roast" is not sufficiently heated in cooking to kill tubercle bacilli (Woodhead). Cattle from the Western plains, and, in fact, all cattle, excluding milch cows, are rarely tuberculous. About 40 per cent. of milch cows are said to be tuberculous, however, and as these are usually slaughtered for "home" consumption, they are rarely, at least in America, properly inspected. For this reason public slaughter-houses where inspection can properly be carried out are of great value.

Tuberculous fowls should be destroyed. Generalization of tuberculosis is much more rapid in the hog, which is frequently tuberculous, and greater care should be exercised in the use of its flesh.[1]

The danger from bread, from uncooked fruits and vegetables, unless handled by tuberculous patients, is so slight that it may be neglected.

**Education.**—Probably the most important and farthest-reaching prophylactic measure is education of the people in matters pertaining to hygiene. In the kindergartens and primary schools short lessons in general hygiene and the danger of spitting upon the floors should be given. In more-advanced schools the lessons may deal with the prophylaxis of pulmonary tuberculosis. The danger of coughing without covering the mouth should be made clear. Organizations among school-children to help keep the streets clean and to further antispitting ordinances have been successful in New York City. Children as well as adults should have the reasons for rules explained to them. It has been suggested, and even put in force in some countries, that a summary of the important elementary principles of hygiene be printed upon covers of school-books. Knopf's excellent rules for school-children are as follows:

Do not spit, except in a spittoon or a piece of cloth or a handkerchief used for that purpose alone. On your return home, have the cloth burned by your mother, or the handkerchief put in water until ready for the wash.

Never spit on a slate, floor, sidewalk, or playground.

Do not put your fingers into your mouth.

Do not pick your nose or wipe it on your hand or sleeve.

Do not wet your fingers in your mouth when turning the leaves of books.

Do not put pencils into your mouth or wet them with your lips.

Do not hold money in your mouth.

Do not put pins in your mouth.

Do not put anything into your mouth except food and drink.

Do not swap apple-cores, candy, chewing-gum, half-eaten food, whistles, bean-blowers, or anything that is put into the mouth.

Peel or wash your fruit before eating it.

Never cough or sneeze in a person's face. Turn your face to one side and hold a handkerchief before your mouth.

Education, however, should not stop in the schools; it should be carried to the adults by means of popular illustrated lectures, at halls convenient to the classes it is intended to reach. Every city should have its permanent tuberculosis exhibit or museum, where at frequent intervals demonstrations should be held. The Tuberculosis Committee of Yonkers, N. Y., has made use of stereopticon pictures, where all who gather in the city park during the evenings may see them. A similar plan is being carried out in New York.

[1] See H. Sessions, Cattle Tuberculosis, for excellent *résumé* of the whole subject of Animal Tuberculosis.

Especial attention must be given to the education of those constantly exposed. It is not sufficient to give the tuberculous patient a few general rules, particularly if he is not very intelligent. Written or printed rules in detail should be left with the attendants, but they should be fully explained orally. In some cases it is wise to tack up a card where it can be seen by all the household and serve as a constant reminder.

**Notification.**—First put in force by Michigan and New York City, in 1893, notification has been widely adopted in America, Europe, and Australia. Voluntary notification should always precede compulsory, although where this has not been done the same results have been reached by not enforcing the compulsory notification. Good results have been obtained by voluntary notification, stimulated by a small fee for each case. The chief objection is the publicity which is supposed to be attached. Laws should be passed making it a serious misdemeanor for the health officer to allow any but a duly authorized official to have access to the records. This would prevent the persecution of patients by patent-medicine firms and by those afflicted with phthisiophobia, which often works great hardships. The public should be informed that notification does not mean placarding the house nor placing any restriction upon personal liberty as long as a reasonable amount of care is maintained.

Pulmonary tuberculosis is a house disease. Not only the fellow-inmates of the house are subjected to great danger of infection, but the succeeding families may be infected. For this reason it is imperative to cleanse and disinfect thoroughly each house which has been occupied by a patient with pulmonary tuberculosis, more especially if he die there. It should be made compulsory upon the patient, his family, and his physician to report to the sanitary officers a change of residence. Proprietors of houses should not be made responsible for reporting a change of residence, as it would quickly work great hardship upon the patients. Any patients who repeatedly fail to notify the proper authorities of a change of residence should be made liable to detention in a sanatorium. The value of notification in relation to inspection and disinfection is difficult to overestimate.

Biggs has found that many physicians who fail to report cases will readily fill out a blank containing the required information, when free sputum examinations are made. In New York no action is taken about cases in private houses or where the physician indicates that he is willing to instruct the patient and family.

**The House.**—"Consumption may well be termed a house disease," writes Flick. "Without the house it would not exist. It depends upon the house for its implantation, propagation, and for evolution of all its phenomena. The house is the place where the tubercle bacillus lies dormant in wait for its new host; it is the place where the new host gets its implantation; it is the place where the tuberculous subject gradually becomes a consumptive; and it is the place where the consumptive dies.

"In studying the progress of civilization in the light of modern science one is struck with the egregious blunders into which man has been led by his desire for privacy and comfort. He has built his house to keep out his enemies, to protect himself from heat and cold, and to screen himself from the curiosity of his neighbor. He has sought to make his home his castle, but in reality he has made it the place wherein he courts death."

Two important factors in regard to the house have long been known to

and insisted upon by sanitary experts, precautions against overcrowding and proper ventilation. A third very important factor has only very recently been introduced, disinfection.

*Overcrowding.*—It has been clearly shown (for London) that the important feature in overcrowding is less the number of inhabitants per acre than the average number per room, and the mortality, further, is lower where each person occupies a single bed. At least 600 cubic feet of air space should be allowed for every adult and at least 400 for every child (Biggs). Dutcher has shown the danger of overcrowding even in cities (*e. g.*, Baltimore) where no tenements occur. The tuberculosis death rate is directly proportional in France to the size of the city (the larger the city the greater the overcrowding), but Graux thinks overcrowding of less importance in Paris than deficient ventilation and sunshine.

*Ventilation.*—Direct sunlight kills the tubercle bacillus in thin layers of sputum in five or six hours and diffused sunlight in several days. It is not, however, so fully realized that proper ventilation greatly facilitates this bactericidal action. The height of the house should not exceed the width of the street. "Back-to-back" houses greatly increase the tuberculosis death rate. Biggs thinks that houses built in lots 25 x 100 feet should not occupy over 60 per cent. of the surface of the lot. Menusier found the death rate more or less proportional to the number of stories. Lodging-houses should be provided with an automatic and adequate system of ventilation not under control of the lodgers. Partitions in lodging-houses, built upon the cell plan, should be raised eight inches from the floor (Kennaday).

A large cubic air space is of little avail if the ventilation be bad (Maxwell), and Ransome states that scrubbing without good ventilation has no effect upon the microörganisms in a room.

For dwelling-rooms 3000 cubic feet of fresh air per head is needed every hour. Adequate provision should be made for parks in all cities. It has been aptly said that in the country the only bad air is in the farmers' houses, whence it seldom has an opportunity to escape. The "devitalized air toxæmia" of Dennison and "ruminated air" are apt and fit terms.

*Disinfection.*—Disinfection of all houses which have been occupied by patients with pulmonary tuberculosis should be made mandatory by law. It should be required each time a patient changes his residence. Sleeping cars, particularly those occupied by patients on their way to health resorts, should be fumigated at the end of each trip. Rooms in hotels occupied by patients should be disinfected on vacation. All disinfection should be performed by the sanitary officials. In open health resorts frequented by patients with pulmonary tuberculosis, each boarding-house or pension should be required to have its rooms numbered, to keep a register of inmates, and to notify the health officers of removal or death of the inmates.

The best means of disinfection for rooms is formaldehyde vapor. At least 8 ounces (250 cc.) of the commercial (40 per cent.) formalin should be used for each 1000 cubic feet of air content. Inasmuch as the efficiency of formalin is directly dependent upon the strength of the vapor it should be vaporized as quickly as possible. The most efficient method is that employed by Biggs, of New York. For an ordinary room (1000 cubic feet) 1 pound (500 gm.) of lime, 8 fluidounces (250 cc.) of formalin, and 2.5 to 3 fluidounces (75 to 90 cc.) of commercial sulphuric acid are required. All openings but the door are sealed. The formalin is poured into an empty

water pitcher, 4 ounces of water added, and the sulphuric acid poured slowly in. The lime is placed in a china or earthenware wash-basin on the floor upon newspapers, all water removed from the room, all drawers and cupboards opened, the mattresses stood on end, and the mixture poured quickly upon the lime and the door sealed. The sulphuric acid may be packed in a tin bucket containing the lime and with the formalin in a separate bottle may be used by any person of ordinary intelligence. The room should remain closed at least six but better for twelve or eighteen hours. Dried masses of sputum should be soaked with a 2 per cent. solution of calcium hypochlorite and carefully removed. Paraform candles are effective for small spaces, such as closets.

In regard to the other disinfectants, commonly employed, much diversity of opinion exists. Phenol (5 per cent.), corrosive sublimate (0.1 per cent.), copper sulphate, and numerous others have proved in many instances unsatisfactory. It should, however, never be lost sight of that after formalin or any disinfectant thorough cleansing is just as imperative. A room which has been thoroughly cleansed and carbolized is safer than a room in which formaldehyde has been used and cleaning neglected. Thoroughly wetting the ceilings, walls, floors, and furniture with 1 to 2 per cent. volume of chlorinated lime (1.5 ounces to a gallon), applied with a Turk's-head brush, gives excellent results. Where this cannot be done, rubbing the walls down with bread-crumbs or dough may be of value.

After death or removal the entire place should be renovated. The model requirements in force in New York City include, besides disinfection, scrubbing the painted woodwork with a solution of hot soda, repainting, repapering or rekalsomining the walls. These methods are efficient in ridding an apartment of tuberculous infection which even with efficient disinfection it is hard to accomplish. They are easily understood, improve the premises, consequently are cheerfully acquiesced in by the tenants and almost always promptly carried out by the owners (Biggs).

*Clothing.*—Hangings, bedding, mattresses, pillows, and rugs should be disinfected with steam. All articles of little value and all old books and papers should be burned. All soiled linen should be boiled. Rabinowitsch and Jacobitz working separately have experimented with different colored paints and have found that tubercle bacilli lived a shorter time on white enamel, which they recommend for use in offices. The disinfection of books in public libraries by formaldehyde gas should be carried out. The books, when returned, should be widely opened and exposed to the concentrated vapors in a confined space for several hours.

*Tenements.*—The tenement house is a hotbed for pulmonary tuberculosis. The "lung-block" of New York, so ably described by Poole, shows what exists in many of our large cities and the urgent need for reform. Model tenements have been erected in many cities and laws governing their construction passed. It is here that ventilation and sunlight are luxuries, that overcrowding is rife. Buildings, hopelessly bad, should be condemned and pulled down. All tenements should be licensed to contain a certain maximum number of individuals (Squire).

**Institutional.**—In all institutions tuberculous individuals should be separated to some extent. Tuberculous patients should be admitted to a general hospital only if no special hospital exists. They should then occupy separate rooms and should under no condition be allowed to enter the general

wards. Hospitals for the insane should have separate pavilions for their tuberculous inmates. Nurses and attendants in such pavilions would often do well to wear masks. Patients with pulmonary tuberculosis should be absolutely prohibited from living in common lodging-houses (Biggs). Church authorities will no doubt soon see that unhygienic convents and monasteries, and unhealthy clergy houses and other ecclesiastical edifices are anachronisms and should be abolished.

**Prisons.**—Mortality from pulmonary tuberculosis has long been so high in prisons and reformatories that sentence for a term of years is almost equivalent to a sentence of death by consumption (Johnston). Tuberculosis is said to cause 40 per cent. of the deaths in prisons (Luzzato). The conditions in the county jails are often much worse than in the penitentiaries. Each prisoner should be examined at once and if found tuberculous should not occupy a cell with a healthy person. After death or removal, the cell should be carefully disinfected. Ransome thinks whitewashing of little value and possibly of danger, through scaling and dust. Tuberculous should not be placed near healthy prisoners in workshops, should have lighter if any work, and the proper disposal of the sputum should be provided for. The State of Texas has established a farm colony (Wynne State Farm) and New York an institution in the Adirondacks for their tuberculous prisoners. Excellent results have been obtained in both institutions. No tuberculous prisoner should be pardoned until his future environment has been carefully considered. Baer has shown that for Germany the tuberculosis death rate in prisons has decreased one-third from 1877 to 1900.

**Schools.**—School-rooms should be well lighted and sunny. The windows should be widely opened during change of rooms or recess. The floors and walls should be so constructed that they can be washed and not swept (dry) or dusted. The school-room should be disinfected every three or four months. Each room should be provided with a sputum box. Hygienic drinking fountains with an upward flow should be placed in every school and the common drinking cup should be abolished. In doubtful cases the books should be disinfected, and it is wise to disinfect all books each year. Slates should not be used. It would be a wise measure to inspect all boarding schools and their staffs at intervals. Tuberculous teachers, scholars, and janitors should be excluded until their sputum has long been free from tubercle bacilli, and unquestionably it is better both for scholars and teachers to exclude them permanently. In Denmark teachers are required to have a new certificate every three months stating that they are not tuberculous. Special schools, held out-of-doors, should be maintained for all tuberculous children. School-rooms should never be used for public gatherings.

**Factories and Shops.**—"The home and the workshop are the two places where environment of sufficient intensity for contamination and contact of long-enough duration for implantation can most readily exist" (Flick). The minimum air space per individual, proper ventilation and lighting, sufficient floor space, the substitution of mopping or washing for dry sweeping, absolute prohibition of spitting on the floor, a sufficient number of suitable cuspidors, proper medical inspection, limitation of hours, and regulation of hours for meals in a suitable place apart from the workshop, removal of gases, vapors, and dust should be established in all workshops. Sleeping in workshops should be prohibited. Occupations entailing much exercise require more ventilation and less warmth than sedentary trades. It is

advisable to paint all walls for two meters (about six and one-half feet) from the floor with enamel paint.

**Trades.**—Some trades are especially dangerous and measures should be taken to protect the workmen. In some countries, *e. g.*, Germany, the liability of the manufacturer is held not to end when he settles claims for injuries to his employees. Industrial insurance will accomplish much if the employers are forced to contribute to the deficiency should one arise. Appliances for removing dust in potteries, glass and stone cutting, polishing and grinding, hoods for noxious vapors, such arrangements of benches and machinery that the workmen will not have to sit or stand for hours in cramped positions should all be provided. Certain trades should be scheduled as dangerous and be absolutely prohibited in sleeping-rooms. Public-houses and saloons are looked upon by Niven as a "large manufactory" of pulmonary tuberculosis. Persons with tubercle bacilli in their sputum should not be allowed to handle or to prepare food for others, nor should they attend non-tuberculous invalids. Dentists should always sterilize all instruments. Coal mining, lime and gypsum working, and tanning have been looked upon as lessening the chances of disease. The trades unions would do well to strive vigorously for these reforms.

**Traffic.**—"Sleeping-car" infection no doubt occurs, but its importance has been exaggerated, although we should not for this reason relax our efforts for clean cars. It will be impossible to segregate tuberculous passengers in separate coaches until a law is passed making it a misdemeanor for them to ride elsewhere, and the wisdom of this is very questionable. Every coach that runs to a health resort should be disinfected with formaldehyde at the end of each trip. The construction should be as plain as possible. The vacuum system of cleaning, by which all dust instead of being stirred up is entirely removed, has been successfully used. Dry sweeping *en route* should be prohibited. The damp cloth should replace the dust pan and brush. Brushing off passengers should be restricted to the rear end of the car or prohibited altogether. The question of cheap individual drinking cups for travellers is of as much moment as any other problem. Prausnitz, in 1894, insisted that little danger arose from cars, but Petit strongly opposed this view. Hamilton found two coaches out of twelve infected with tubercle bacilli.

Street railway cars, "electrics," trams, and omnibuses would seem to be a grave source of danger. Flick states, however, that after some investigation he fails to find pulmonary tuberculosis more prevalent among conductors of these cars than among the general population. The majority of such conveyances are wretchedly ventilated and disinfection is rarely if ever carried out except for smallpox. Dry sweeping is the method nearly always employed for cleaning. The vacuum system should be introduced.

Officers of passenger ships should be warned of the necessity for careful disinfection of all cabins occupied by "coughers."

**Hospitals.**—Many competent observers hold that the great reduction of and the low mortality in England are due to the establishment of hospitals for patients in far-advanced stages. These institutions are by far the most important in the antituberculosis crusade. Infection when happening usually occurs from those in the last stages. If for every patient provided for in this way one less individual be infected, it is but a matter of a moment to figure out a great reduction in mortality.

Such hospitals should be founded by every municipality of 100,000 or more inhabitants. They should be situated in the healthy, wooded suburbs, and easy of access. Further provisions for the open-air treatment should be made, for, as Letulle says, isolation without attempt at cure is deplorable and cruel. The grounds should be inviting and no opportunity spared to make the whole institution as attractive as possible. The average stay in such institutions may be said to be about six months.

When after notification the sanitary inspectors feel that proper precautions cannot be taken by the family in the case of a very ill patient, or that the patient insists upon breaking all prophylactic measures, if necessary he should be removed to the institution. It is safe to say that such a course will have a deterrent effect upon the most refractory patient and that actual forcible removal will seldom be necessary. The constitutionality of such a procedure is easily justified, as it is *pro bono publico*, and the healthy have more rights than the sick.

**Dispensaries.**—Next in regard to prophylactic value stand the tuberculosis dispensaries, aptly termed preventoriums. Their chief value lies in their educational opportunities. The dispensary physicians should after careful consideration decide what is best for each patient. He should be visited at home and fully instructed in hygienic measures. Other members of the family should be examined if necessary. Sputum cups should be freely supplied and full instructions for burning them be given. Printed directions for the patient and for prophylactic measures for the family should be fully explained and left for reference. Where these instructions cannot be carried out the patient should be advised or persuaded to go to the hospital or sanatorium. If he refuse, a special report should be made to the board of health. A further advantage of the dispensary is that any person, however poor, can have expert medical advice.

**Sanatoriums.**—The value of sanatoriums lies chiefly along two lines, education and arrest of patients in the "closed" stages. Extensive statistics show that about 43 per cent. of patients with tubercle bacilli in their sputum ("open" cases) lose them during sanatorium residence. While 60 per cent. of the "open cases" still have tubercle bacilli in their sputum on discharge, the education they have received in the sanatorium renders them so careful that in most instances they are of little or no danger. Sea-side sanatoriums for children are most important, but day sanatoriums which receive advanced cases have a great value. "All-night" sanatoriums or hospitals where patients who are still able to work can remain under supervision and sleep out-of-doors are very valuable for the single and for those whose homes afford no such advantages.

Any danger of sanatoriums to the surrounding community has yet to be proved; indeed, the health of the community is often improved. The better mode of life that is customary in health resorts has much to do with the lessened death rate from tuberculosis in these localities.

The municipal campaign against pulmonary tuberculosis as outlined by Biggs should, therefore, include: "(1) Compulsory notification; (2) suitable plans for the education of the people, including visitation and instruction of cases, especially in tenements, lodging-houses, boarding-houses, and hotels; (3) a complete and efficient scheme for disinfection and renovation of premises after death or removal; (4) supervision of shops, occupations, and conditions where consumptives are employed; (5) a hospital equipment, consisting of

a reception pavilion for patients, suitable institutions within or near the city limits for the care of advanced, and a country sanatorium in a well-situated locality for incipient cases; (6) power of compulsory removal and retention in hospitals when necessary.

The addition of one or more dispensaries for pulmonary tuberculosis, situated in the midst of the poorest and most thickly populated districts of the city, in easy access of the street railways, would make such an organization nearly perfect. The organized charity bodies of all cities have an important part in the struggle, as poverty and tuberculosis are directly connected. The lower the average income the higher the tuberculosis mortality, and conversely (Gebhard).

**General Prophylaxis.**—General prophylaxis dealing with sputum, its collection and destruction, coughing, rules for the tuberculous patient, and the cleaning of the house, strike at the fountain head of infection. If we could cut off the supply of infectious material from patients, infection would soon be reduced to the vanishing point (Woodhead). This deals largely with the tuberculous patient and the disposal of his sputum.

**Expectoration.**—Careless expectoration is the chief source of infection. Laws should be passed in all cities prohibiting spitting upon the pavement, the floors, or steps of public buildings, of elevated railway platforms, of waiting-rooms, of all cars and steamboats, especially ferries, of wharves, public carriages, places of public entertainment, cafés, restaurants, shops, hotels, prisons, and boarding-schools. These laws should be posted in all such places. It is not enough, however, to pass such laws—they must be enforced. No community has worse laws than it deserves and the enforcement of all laws is in the hands of the people. Not until public opinion is aroused and the public educated up to the fact that sputum is as nasty, as loathsome as, and in most cases more dangerous than, other dejecta (urine and fæces) can the spirit of antispitting laws be carried out. It is useless to try to prevent patients with tuberculosis from expectorating and allow the general public to do so. Nuttall has estimated that several billions of tubercle bacilli may be expectorated in twenty-four hours by a single patient (7,200,000,000 by Cornet). It is fortunate that tubercle bacilli rarely if ever multiply outside the body.

**Disposal of Sputum.**—It is not enough, however, to say "No spitting here." All such signs should be accompanied by others, indicating where to spit. All persons should be advised to spit only when necessary and then to deposit the sputum, if at all possible, in water. Patients should be told that it is for their own interest not to expectorate except into a proper receptacle. That the only dangerous sputum is dried sputum cannot be too often emphasized. For this reason sputum should always be deposited in the gutter and not upon the pavement or crossing.

Spittoons should be provided in all public buildings, places of assembly, cars, and along all stairways. They (1) should be of metal or unbreakable material (to avoid infection by scratching), (2) should, as far as possible, conceal the sputum, (3) must not allow their contents to spatter, must be placed breast high, (4) must be easy to clean and hard to upset. They should be 14 cm. high and 22 cm. in diameter at the opening and 16 cm. below. The lower opening of the funnel should be 3 cm. from the bottom and 8 cm. in diameter. The ordinary slop-jar answers these requirements much better than the spittoons ordinarily employed. Spittoons should contain some

antiseptic fluid, preferably one that digests or dissolves the sputum, although plain water will answer. Sand, bran, sawdust, or ashes should never be put into receptacles for sputum. The caustic alkalies in strong solution are very efficient.

Spittoons with constantly running water are excellent for the general public, but should not be used in sanatoriums or hospitals.

Sputum should be carefully guarded from flies, which may widely disseminate the tubercle bacillus.

The advisability of doing away with spittoons in physicians' offices, dispensaries, and sanatoriums should be carefully considered. It is not necessary for physicians, even in health resorts, to have spittoons in their offices. A few paper cuspidors, under a notice stating that every patient who expectorates should have a pocket cup, are far more cleanly, less disagreeable, just as practicable, and emphasize a most important measure. General sputum boxes or spittoons in sanatoriums lead to carelessness, are often the seat of accidents, and should be abolished. Everyone should be encouraged to use sputum boxes when suffering from pneumonia or other even slight respiratory diseases. This would help much in dispelling the foolish prejudice against the users who at present, when trying to protect others, are shunned and ostracized. These foolish and dangerous ideas must be strongly condemned.

A perfect pocket sputum cup or flask has not yet been devised. Many patterns have been put on the market, but none are much better than Dettweiler's. The essential points of a good pocket cuspidor are that it should be easily managed, preferably with one hand; perfectly tight; not too bulky; easily cleaned, and so constructed that sputum does not adhere to the cover when opened.

The "cup" devised by Major D. W. Appell, U. S. A., consisting of thin, impervious cardboard so folded as to form an envelope which contains a bit of cotton, is very satisfactory for patients who expectorate but little or for use while walking. The main objections to it are the filaments of cotton that float off in the air each time the box is opened, the small capacity, and the tendency to spill unless always carried upright in the pocket. The "sanitary cuspidor," consisting of a metal (tinned-iron) frame, holding a waterproof thick paper cup, so folded that flanges prevent spilling if accidentally overturned, is probably the best for use at home and in sanatoriums. The advantage of both these cups is that they need little handling and can be burned daily. They do not need to contain any fluid, and the bed-room or porch cup can be filled with sawdust, which facilitates burning and prevents spilling on the way to the crematory. The papers in the metal frames should be changed daily, the cup filled with sawdust and wrapped in paper and placed handy (in a special box) for collection by an orderly, who should wear rubber gloves. The metal frame should be washed in carbolic each day.

The use of cloths or Japanese napkins is not to be recommended, but is at times necessary for the very ill or very poor. Each cloth or napkin should be used but once and immediately deposited in a paper bag or a newspaper folded into a bag. This helps to prevent drying, does away with a second handling, and facilitates burning. If the patient is in bed the paper bag may be pinned to the side of the bed; if up and about the papers or cloths may be put temporarily in a pocket with a detachable rubber-cloth lining, which admits of disinfection, or in a chatelaine bag.

Japanese napkins may be made impermeable, by a method devised by Locke: "Dissolve with gentle heat 2 ounces of cera alba Japonica, 1 ounce of paraffin (or spermaceti) wax in about 10 ounces of turpentine. Spread a thickness of about a dozen serviettes on a non-absorbent surface and brush over with the warm solution until well saturated. Separate and hang to dry for a few days. A better but more expensive solution is prepared as above with the addition of a small quantity of pure rubber thoroughly dissolved in turpentine." This is hardly necessary, however.

If cloths or paper napkins are used, the hands should be frequently washed, for Baldwin has shown that unless the patient is scrupulously clean the hands are frequently soiled. It is needless to add that the handkerchief should never be used for sputum nor should it be employed to wipe the lips after expectorating, but a special cloth should be kept for this purpose.

Sputum may be disinfected by heat (burning, boiling, steaming) or by chemicals. The best method is by burning, which may be done in a special crematory or one connected with the general heating system. In the home the kitchen stove and a hot fire are all that is necessary. The boxes should be carefully placed upon the fire. Fluegge has advised mixing the sputum with ½ liter of coffee-grounds (or sawdust) and 100 cc. of solution of saltpetre in water (1 to 5). Sawdust or peat is amply sufficient.

Boiling when used should be continued thirty minutes, as Moeller has shown that ten minutes is not sufficient. Disinfection with live steam is efficient and renders the sputum fluid, but is expensive, as it cracks a certain number of the glass cups and destroys the rubber stoppers. The manipulation in boiling is very disgusting, requires one-half hour, and the vapors are very unpleasant.

Destruction by chemical means is usually expensive and not always efficient. Antisputol, of Gertner, consisting of 100 parts of peat and 15 parts of saturated aqueous solution of copper sulphate and 2 per cent. of formaldehyde, does, he believes, penetrate into the masses of sputum. Watery emulsions of creolin are uncertain and unstable (Hueppe, Gerlach). Lysol is not fully soluble in water, has a disagreeable odor, causing headache (Leube), but in 2 per cent. solution is efficient in twenty-four hours (Hautefeuille). A 2 per cent. solution of chlorinated lime is efficacious when mixed with an equal quantity of sputum (Délèpine). Izal emulsion (1 to 60) disinfects equal quantities of sputum (Délèpine and Coutts). Lysoform is less disagreeable and less antiseptic, but more expensive than lysol. Kresol, sapocresol, saprol, and solutol fail to disintegrate the sputum masses. Lysol acts much better. Sodium or potassium hydrate readily dissolves and disinfects sputum, but is poisonous. Carbolic acid (5 per cent.) is effective in twenty-four hours if stirred, and mercuric chloride (5 to 1000) is of value (Steinitz).

The emptying of sputum cups into drains or water-closets should never be permitted in hospitals or sanatoriums. The experiments of Musehold have shown that putrefactive organisms have little effect upon the tubercle bacillus, which may live in drain water for 194 days. Moeller's work has shown the danger of throwing sputum into sewage-disposal plants, especially where the water is afterward used for irrigation. He found tubercle bacilli on radishes.

**Coughing.**—Patients should always hold a cloth (not the hand) before the mouth on coughing or sneezing. This cloth should be frequently

changed and burnt and not used as a handkerchief. Von Ruck suggests that these cloths be soaked in a 5 to 10 per cent. solution of glycerin in water. Chairs, working benches, and beds should be at least four feet apart. Alkaline antiseptic mouth washes should be frequently used for their cleansing effect upon the buccal cavity. Koeniger thinks a fine spray is ejected in talking, in proportion to the sharpness of pronunciation of the consonants, but this cannot be guarded against. The danger from "shaking out," before using a handkerchief or cloth in which tuberculous sputum has been deposited, is probably a more serious menace than the droplets from coughing. Telephone mouth-pieces should be cleansed frequently and the cheap paper disks, made to cover them, deserve wide use.

Fæces and urine, even when the alimentary and genito-urinary systems are apparently free from tuberculosis, often contain tubercle bacilli. For disinfection, chlorinated lime, carbolic acid, or burning should be employed.

**Rules for Patients.**—All patients should be instructed about personal cleanliness, and they should be fully alive to their duty to the public, for until this is realized little effective prophylaxis can be accomplished. Beards and moustaches should be worn short, if at all. Kissing should be forbidden. The hands should be frequently washed and the patient cautioned about touching any articles of food intended for others. He should cough into a cloth and always turn his head when doing so. Carelessness about the sputum should not be tolerated. The patient should have his own bed, four feet distant from another, and, if at all possible, his own room. It is unnecessary, when the patient comes to the table, to have special dishes and silver if care be exercised in washing, but when confined to bed his tray and dishes may be kept apart and washed separately. The patient's room should be carefully cleaned, never swept, and 5 per cent. carbolic acid solution used freely. Disinfection of both room and clothing of the well-to-do patient when any possibility of infection has previously occurred is not without its advantages. The room should be furnished with washable curtains; carpets and draperies should be removed and one or two rugs provided. The blankets should have washable covers (Cornet). The walls should be painted, preferably with white enamel. The patient should have the sunniest, best-ventilated room in the house.

**House.**—The site of the house should be carefully considered. Dampness is conducive to pulmonary tuberculosis, and the soil and subsoil, therefore, should afford ample drainage. The cellar should be cemented. Sun should enter every room at some time whenever possible, and the house should face southeast or southwest. There should be no inside rooms and all rooms should have two windows. The window area should be at least one-seventh of the floor space. Too many trees should not be permitted close to the house. "He who plants a tree in front of his house begins to dig his own grave" (Indian proverb). Dry sweeping should be abolished and all brooms covered with bags which have been moistened in some antiseptic solution. After using, the bags should be boiled. The mop should replace the broom. Feather dusters should never enter the house. Damp cloths should be used for the "pernicious process aptly termed 'dusting'" (Osler). Polished furniture should be wiped with oiled cloths. Both mops and cloths should be boiled or soaked in some disinfectant.

**Laundry.**—The infection of workers in laundries can be prevented. In all hospitals and sanatoriums the personal and bed linen should be handled

as little as possible. It should be placed in bags, and, on reaching the receiving-room of the laundry, put in the sterilizer, which should be the only communication between the receiving and assorting rooms. All blankets, pillows, and mattresses should be disinfected with live steam and formalin. Blankets can then be washed. Especial care should be taken of handkerchiefs, which should always be gathered in bags and disinfected.

**Servants.**—The danger of infection from tuberculous house servants is not sufficiently appreciated. The close confinement, the small, poorly lighted, and wretchedly ventilated rooms for servants often act like a boomerang. The rich can prevent the spread from but not to their homes.

**Domestic Pets.**—Fondling or kissing parrots, dogs, cats, or canaries may in rare instances transmit tuberculosis, but the danger is slight for the healthy. For the tuberculous subject the danger of secondary infection should lead to caution about such habits.

**Churches.**—It is a natural instinct, that, as man realizes that human aid is of no avail, he should turn to the church. Bishop Fano, of Italy, realizing this danger, has recently issued a circular to priests, advising the use of sawdust in sweeping, and the washing of the grate of the confessional with lye once a week. The use of individual communion cups, which should be carefully cleansed after use, is growing rapidly in America and should be encouraged.

**Burial.**—It has been urged that all tuberculous bodies should be cremated. While some very slight danger may arise from the bodies of tuberculous animals, buried at an insufficient depth, such danger may be neglected in the case of man.

**Individual Prophylaxis.**—If general prophylactic measures could be perfectly carried out there would be little need of individual prophylaxis. The very nature of the disease, its simulation of catarrhal bronchitis and other benign diseases, however, will always make individual prophylaxis of much importance. To two classes it is of especial value, to the very young and to the predisposed. For the latter it is a struggle to escape tuberculosis in some instances from the "cradle to the grave."

Prophylaxis should begin at birth, especially if the child come of parents weakened through any disease. If the mother be healthy she should by all means nurse the child. If the mother be the subject of tuberculosis she should not nurse the child, both for her sake and the child's. If the child be predisposed, *i. e.*, come of tuberculous or weakened forebears, no means must be omitted to strengthen and harden it. The baby should be given over to a healthy nurse and its intercourse with the tuberculous mother should be as limited as possible. In no case should it occupy the same bed. The milk should be "certified" and modified to suit the child's need. If not "certified" it should be heated to 180° to 190° F. The nursery should be the sanctum of every household and visitors should not be allowed to enter it. The children should be brought down to the visitors, and they should be taught not to kiss strangers and to keep everything out of their mouths. It is a wise plan to taboo street shoes and trains from the nursery. It is here that dust should never be found. At first the child may be confined to a clean blanket placed upon the floor, but this is not possible later. He creeps and crawls everywhere in the room. The bacterial flora of the floor is soon to be found on his hands and under his nails. What is on the hands of children is soon in their mouths. Every

little draught and every little movement of any kind stirs up the dust, often just high enough for the crawling baby to inhale it. The floor, therefore, should be scrupulously clean and with as few cracks as possible. A heated tile floor with tiled walls makes an ideal nursery. A broom should never enter this room, which should be bright, sunny, and well ventilated. Children should never be allowed in a consumptive's room unless it be for only a moment.

In the third to the fifth year the child should be gradually accustomed to cool and then cold sponges, given while standing in warm water. The house temperature should be 65° to 68° and the air not too dry. The nursery should be flushed several times a day with fresh air and a window should be constantly open at the top, day and night. For the predisposed hyperventilation is necessary. It is often well to have a second room, which the children can use for a few hours every day, and it is always preferable that the attendant sleep in an adjoining room. Children if not too warm seldom throw off their coverings. The hours out-of-doors, especially for predisposed children, should gradually be lengthened in winter and should be nearly as continuous as in summer. The ideal place for such children is the country or an open suburb. If not strong when the school age arrives, all thoughts of indoor study should be abandoned and interest aroused in nature. These children are often precocious and quickly catch up to their fellows later.

Nasal obstruction causing mouth breathing should receive appropriate treatment. Every effort should be made to keep the mucous membranes healthy. Lepelletier advocates nasal irrigations for all predisposed children and Jacobi for catarrh and swelling of the cervical glands. Care of the mouth is very important and all carious teeth should be removed at once. During convalescence from infectious or other diseases great care should be exercised. If anæmic, cod-liver oil, syrup of the iodide of iron and arsenic should be given. Great care should be taken to see that children are not too much bundled up, especially about the neck, which is often the cause of colds through overheating. Tight collars or clothes of any sort are bad. For girls the clothing should be largely supported from the shoulders, and in young women from the hips.

At an early age these children should be taught self-restraint and unselfish habits. The chances of escape or recovery from pulmonary tuberculosis are often lessened by neglect of this rule. In this work of individual prophylaxis the family physician plays the most important part. The Society for the Protection of Children against Tuberculosis, founded in France by Grancher, has for its objects to place the still healthy children of tuberculous families with healthy families in the country and keep them there as long as possible between their second and fourteenth year. At present 250 children in ten colonies are provided for at one franc a day and no child has developed tuberculosis. This example should be followed in all countries as its value cannot be overestimated.

The employment of tuberculous midwives, the practice of ritual circumcision by a tuberculous rabbi, tasting the child's food, chewing it before feeding, or blowing upon it, are all strongly to be condemned.

As the child grows older he should be taught to hold himself properly and outdoor sports of all kinds should be encouraged, but care taken to regulate them to his strength. A well-ventilated gymnasium is excellent for exercise

(during the winter months) in bad weather. Special exercises leading to increased development of the chest and lungs are valuable. They should always be taken in the open air or before an open window.

Plain, simple, nutritious food is of great value. Milk and easily digested fats, such as cod-liver oil, should be freely used. Especial care must be taken of bad eaters, for these are very susceptible (Brehmer).

Change of climate, a sojourn at the seashore or in the mountains, is of great assistance to many youths and girls, especially about the age of puberty. Long sea voyages and ranching are also good. These are especially valuable just about the age at which other members of the family have developed the disease. Doenitz has proposed tuberculin treatment for all predisposed individuals. Any individual who is ten pounds or more under weight should take precautionary measures in regard to pulmonary tuberculosis.

**Choice of a Profession.**—The choice of a profession for predisposed individuals is a difficult task. They should if possible choose an outdoor occupation which does not entail too much exposure to inclement weather. A change from an outdoor to an indoor calling often results disastrously, and Burgeois has called attention to the danger of the city for rural inhabitants.

From a study of the United States census for 1900, the following classification of trades and professions in regard to pulmonary tuberculosis may be made:

Healthy: Clergymen, farmers, planters, farm laborers, lumbermen, raftsmen, millers (flour and grist), bankers, brokers, officials of companies, lawyers, physicians, surgeons, policemen, watchmen, detectives, hotel and boarding-house keepers, collectors, auctioneers, agents, merchants and dealers, gardeners, florists, nurserymen, vinegrowers, blacksmiths, and schoolteachers.

Unhealthy: Bakers, confectioners, hucksters, peddlers, saloon- and restaurant-keepers, iron- and steel-workers, livery-stable keepers, hostlers, musicians, music-teachers, mill and factory operatives (textile), draymen, hackmen, teamsters, tinners, tinware-makers, leather-makers, cigar-makers, tobacco-workers, servants, book-keepers, clerks, copyists, barbers, hairdressers plumbers, gas- and steam-fitters, compositors, printers, pressmen, marble- and stone-cutters.

For girls the problem is more difficult. The majority of outdoor professions entail roughness and lack of suitable companionship.

**Amusements.**—Many places of amusement are poorly ventilated, overheated, and improperly cleaned. Predisposed individuals should not frequent them too often. Their amusements should lead them into the open air. Games of all sorts should be cultivated. Alcoholic and sexual excesses are especially dangerous.

**Marriage.**—Marriage for persons with tuberculous forebears need not concern us if the individuals are robust. If the contrary be the case they should be cautioned about excesses, and the woman if weakly should be warned of the danger of frequent pregnancies.

In regard to marriage of the tuberculous, it is certainly wiser to postpone it until the tuberculous individual has been well for two years. The financial condition should be considered carefully. In the well-to-do, where worry and care about money matters will not enter, marriage should be more readily sanctioned than in the poor, where anxiety for the wife and babies may prove to be too much for the tuberculous husband or the care of home

and children too exacting for the tuberculous wife. Under the latter condition it is certainly wiser to avoid conception. An unhappy marriage greatly increases the chances of relapse or infection.

The danger of infection of healthy individuals who have married tuberculous patients has been much discussed. Weber's cases of tuberculous husbands losing several healthy wives through tuberculosis have been much quoted. Thom believes that such infection is very rare. This danger, though not great, is undoubtedly real. Great care, however, should be exercised and no prophylactic measure omitted. Kissing should not be practised. The danger of infection by coitus is very slight, though Thom ranks it next to kissing. Some explain by this means the greater frequency of infection of wife from husband than husband from wife. Tuberculosis is so rarely transmitted before birth that such danger can be neglected. But every day after birth the danger from infection increases.

**Results.**—The result of any prophylactic measure in tuberculosis is difficult to determine. The incubation period is long and indefinite, and the period of infectivity begins usually long before diagnosis. The decrease of mortality began in many places before the discovery of the tubercle bacillus, and in London has not decreased any more rapidly since. Without doubt were pulmonary tuberculosis treated now as leprosy was in the middle ages it would in a few generations be greatly reduced. It is unfair to compare tuberculosis with leprosy, for, as far as is known, leprosy exists in no animals, while tuberculosis is rife among cattle. The results in Norway, where the strictest measures in regard to notification and isolation have been enforced, are not as yet very startling. Dewez places the reduction due to these measures as 15 per cent. The results obtained in Havana during the American occupancy were remarkable; from 1282 deaths in 1899 the number was reduced to 881 in 1900. Ascher has made a careful study of the reduction of tuberculosis in Prussia and finds it greater in the circles in which no efforts have been made to combat it.

The first results in State prophylaxis are to be seen in the infant tuberculosis mortality, which in New York, as Biggs has shown, is remarkably reduced, from 0.67 per 1000 of total population in 1883 to 1887 to 0.34 in 1898 to 1902. The low mortality among the Southern negroes while in slavery stands out strikingly when compared, as May has shown, with the mortality in this race to-day.

## TREATMENT.

There is probably no chronic organic disease which shows greater tendency to repair and recovery, but this very tendency is fatal for many patients. There is no disease that yields so quickly to such slight efforts on the part of the physician and no disease which progresses so steadily to recovery in the face of so much injurious treatment.

However, these favorable results do not always obtain and the enthusiasm of both patient and physician is often severely tried. The time allotted to the treatment is almost invariably too short, and many patients lack enough persistence to regain their lost health. Another most important factor, really a serious danger, is that many patients in a few weeks enjoy a feeling of almost perfect health. If a patient felt ill and weak until a full

recovery were effected, the percentage of recoveries would be many times increased. As Babcock has aptly termed it, this is the "danger time" in pulmonary tuberculosis.

There is no specific for pulmonary tuberculosis. The hygienic-dietetic treatment is almost a specific for the general condition which, with such treatment, soon equals or even surpasses any state ever reached in health. With the lungs, however, it is a different and a vastly more difficult problem. To change, to arrest, to cure a pulmonary lesion requires not weeks or months, but years. The first part of the time should be passed under careful medical supervision; the latter may be devoted in part to work.

The success of a physician in treating pulmonary tuberculosis depends largely upon his ability to deal skilfully with the physical, psychological, and sociological problems that arise in each case. Each patient must be individually studied. His former habits, pursuits, and idiosyncrasies must be carefully noted. He should be told at once that he has pulmonary tuberculosis, for the shock is soon over. The details of the treatment must be fully gone into and the importance of implicit obedience impressed. He should be told that in conscientious observance of minutiæ lies health, and the reason for every rule should be made clear. "Let it never be forgotten that the patient is to be our partner and coworker in his own case and that a partnership in which one member is ignorant of the course of the business is sure to end in failure" (Minor). No question bearing upon his treatment is too trivial to be discussed, but he must not be allowed to dwell in introspection. The physician and patient must run a "closed corporation," whose affairs should never be discussed by anyone else. The duration of treatment is difficult to estimate and varies much with the object in view, *i. e.*, whether improvement, arrest, or cure be aimed at. Three months is the shortest period from which any permanent benefit can be derived, and this only in the earliest stages. As the disease advances much longer periods are necessary, and two or even three years may be required.

The clothing must not be too heavy. It is impossible to lay down any rules upon this point on account of idiosyncrasies. Sensible perspiration and chilliness are equally dangerous. Wraps should always be at hand. Linen or woollen underwear is to be preferred, and chest protectors and chamois waistcoats under the shirt should be strictly forbidden. Water-proof clothing should be avoided during warm weather, but the feet must be kept dry or dried at once on return from exercise. Damp clothing should always be replaced at once by dry. Hats may or may not be worn, but the head must be protected from the hot sun. Corsets should never be worn tight, and for some patients Ferris waists are much to be preferred. The same garment should never be worn for more than twelve hours (*i. e.*, night and day) without thorough airing.

Patients subjected to life out-of-doors and to hydrotherapy soon acquire resistance to colds and to other slight infections—a process now known as "hardening."

The details of the daily life for a patient may be simply stated as follows:

7.00. Awake. Milk (hot if desired) if necessary. Cold sponge.
8.00. Breakfast.
8.30. Out-of-doors.
10.30. Lunch when ordered.
11.00. Exercise when ordered.

1.00. Dinner. Indoors not over one hour, less if possible.
3.30. Lunch when ordered.
4.00. Exercise when ordered.
6.00. Supper.
7.00. Outside on good nights.
9.00. Lunch and bed.

Once or twice a week a hot bath, followed by a cold sponge.

**Hygienic-dietetic Treatment.**—This has long been called the "sanatorium treatment," as it was first carried out in these institutions. Briefly, it may be said to consist of good nourishing food in proper amounts, of fresh air by day and night, and of exercise and rest properly regulated for each patient. To carry this out seems simple, but the task is often difficult, and much ingenuity, much patience, and unlimited enthusiasm are necessary. Ambitious patients must be restrained, lethargic enthused, nervous quieted, and morose cheered. The vis medicatrix naturæ works well, but very slowly and too much must not be expected of it.

Fresh air, next to good food, is the most important factor, but this estimate of its importance may be said to rest upon empirical grounds. Fresh air stimulates the hæmatopoietic functions, the nervous and digestive system, as well as many other organic functions.

The number of hours spent out-of-doors varies for the individual, the climate, and the season. In summer individual peculiarities are of less moment and nearly every patient can spend day and night out-of-doors. In winter, especially in cold climates, many patients find it impracticable to spend more than eight hours out-of-doors. Senseless exposure must be avoided.

The hours out-of-doors should be spent on a comfortable reclining chair or bed on a veranda, never deeper than its height, facing southerly in winter, northerly in summer, well protected from wind, but freely open to the air and well lighted artificially for use after dark. Liegehallen, much used in Germany, where verandas are opposed on the grounds that they darken the rooms, are long, low sheds with open fronts, protected backs and sides, containing windows and so constructed that the flat roof, slanting backward and downward, is at a height in front which equals the depth of the building (usually ten to twelve feet). The patients, at least four feet apart, occupy these shelters throughout the day. Most recently many observers feel that it is wiser in all acute cases, and for many nervous patients, to employ separate balconies or at least divided porches where each patient can be at perfect rest out-of-doors.

Of most value in dry climates, tents may become very disagreeable in moderately humid climates and, unless especially constructed, are very poorly ventilated. Notwithstanding many intricate devices for ventilation, the best tent (and the cheapest) is the ordinary wall-tent, on a framework, so constructed that the wooden floor is raised one to three feet above the ground, a space of three inches being left between the sides (boarded up to two or three feet) and the canvas walls, which are so arranged that they can be lifted up to the eaves on all sides. This arrangement changes the tent into a covered veranda. Every tent should be supplied with a small stove, a veranda in front and a fly extending well out over the veranda.

Various devices to replace tents have been suggested, but on the whole the veranda where the patient can live, eat, and sleep is by far the best. Many

patients living in cities are unable to have access to a balcony, a back yard, or even a roof. Living in apartments or tenements with three or four flights of stairs to climb, it is almost impossible for them to get into the open air. Sitting wrapped up by the open window during the day and sleeping in a window tent at night must suffice for many.

Sleeping out at night, first brought into prominence by Millet, who employed it for patients who during the day worked indoors at their trade, has long been in use on the Western plains and occasionally by Squire, of London, for about fifteen years. During the last six years it has been extensively employed at the Adirondack Cottage Sanitarium (by fully 50 per cent. of the patients) without any appreciable difference in the immediate results of treatment. For patients who must work indoors it is invaluable. The night air of cities is the purest air. Patients who are ill and who may require the services of a nurse (night-sweats, hæmoptysis, etc.) should sleep out only under exceptional circumstances. The "lean-to," devised by King, is so constructed that the patients sleep and live out-of-doors on deep, covered porches, extending out on both sides from central living- and dressing-rooms. Bathing and heating facilities, and a small room, whither a patient taken suddenly ill can be moved, are essential to this structure.

**Rest and Exercise.**—The proper regulation of these is most difficult. It is always wise to err slightly on the side of rest, but many patients return to their former occupations with their muscles in such a condition, so soft and flabby, that relapse is indelibly written upon them. The rest treatment has unquestionably of recent years been enforced too long in many cases.

The value of rest in all acute and subacute stages of pulmonary tuberculosis is now fully recognized. Exercise to the point of fatigue results in an auto-intoxication, increased disintegration of albumin, and lessened assimilation. It is useless to attempt forced feeding in a febrile patient who is not at rest, and in any case it is wisest to put the patient at rest out-of-doors for the first few weeks of treatment.

The rest at first, particularly in febrile patients, should be absolute (in bed on a private porch). All business cares, letter writing, study, prolonged or exciting conversations, should be forbidden. For a time the patient should see few visitors. Overexercise *en route* to or on arrival at a health resort is frequent and physicians sending patients away from home should carefully guard against it. At the end of two or more months exercise should be begun in suitable cases and thereafter the problem resolves itself into getting the patient into "condition." Without exercise, when it should be taken, it is possible that the organic cells whose vitality is lowered cannot resist fatty infiltration. Exercise is, therefore, most important in order to produce healthy persons and not a crowd of convalescents.

Passive exercise by massage may be begun when the patient is still confined to bed, before the temperature is fully normal and when the loss of weight is still marked. It should be carefully watched and cause no fatigue. Massage is contra-indicated in great bodily weakness, acute exacerbations, hæmoptysis, severe complications, and intercurrent diseases.

Active exercise should be begun as soon as possible. It is wise to furnish every patient with a few simple printed rules for exercise, such as the following:

(Exercise means walking. Special permission must be obtained before indulging in other forms of exercise.)

None for one week after beginning treatment, then ask about it.
None if feverish.
None if blood in sputum.
None if loss of weight.
None if fast pulse.
Never get out of breath.
Never get tired.
Never run.
Never lift heavy weights.
No mountain climbing.
Go SLOW.
Exercise regularly and systematically, whether rain or shine.
Walk up hill at start so as to come down hill on return.
Remember always that you will have to return.
Rest one-half hour before and after meals.

Much difference of opinion exists as to the best time for exercise. Some advise it immediately after meals, others between, but all agree that rest out-of-doors before meals is essential. For patients with a weak digestion, rest for one-half hour after meals is often of great value.

Exercise should always be taken out-of-doors, and the best form to begin with is walking on the level either alone or with two or three companions at a rate of two miles an hour, with frequent pauses for rest. It is wise to begin with five minutes in the morning and gradually increase in suitable cases a few minutes each week, until at the end of the treatment the patient is able to spend four to six or more hours each day on his feet without fatigue. Inclines should not be attempted until the patient can walk one-quarter to one-half hour on the level. In some instances carriage riding for a definite short time, or a short boat ride, may be allowed when the patient is able to walk but a few minutes. Tennis, rackets, foot-ball, base-ball, hockey, lacrosse, hand-ball, polo, fox hunting, wrestling, fencing, boxing, gymnastics (except light calisthenics), and all other violent sports should be avoided. Golf (without the full swing), croquet, fishing and hunting (not entailing too much exercise), gentle bicycle riding (on the level), rowing or paddling, skating (for those proficient), skeeing, snow-shoeing, swimming (in great moderation), and horseback riding may be indulged in with moderation, when the disease has been arrested for some months. It cannot be denied that many patients who after recovery do indulge in violent exercises remain well, but more relapses occur from overexertion in sport or games than from work. The amount of exercise that any patient can finally arrive at depends upon his former habits.

There are four chief contra-indications to active exercise: (1) Fever, (2) rapid pulse, (3) blood in the sputum, and (4) loss of weight. While these symptoms cover nearly every case, in a few patients great dyspnœa on the slightest exertion, marked weakness, gastric disturbance, increased cough and expectoration, and increase of physical signs, are also contra-indications to exercise. A subnormal temperature (oral) in winter is of little moment in regard to exercise, when the general condition is satisfactory. A rise of temperature (rectal) to 101°, which after one-half hour of rest falls to 99.5° or lower, does not contra-indicate exercise. The effect of over-exertion is often a lowering of the oral temperature on the same day, while

the rise does not manifest itself until the second or even the third day. The pulse should be taken before arising and at rest. When at any time it reaches or exceeds 100 per minute, exercise should be taken with great caution and the pulse carefully and frequently noted. A pulse of 110 or over at any time of the day while at rest is a contra-indication to any exercise, even dressing. These statements, however, do not refer to a patient who is just convalescing from an acute attack, when some cardiac weakness is expected. Lessening the amount of food, especially milk, if in excess, often reduces the pulse rate (Fanning).

*Respiratory Exercises.*—The value of pulmonary gymnastics is not yet definitely determined. On the one side all unnecessary movement of the lungs is forbidden, and artificial pneumothorax, a plaster corset or adhesive strapping advocated. On the other, some go so far as to recommend active pulmonary gymnastics in subacute stages.

Respiratory exercises may be passive or active. Among the former may be mentioned the use of the pneumatic cabinet, manual pressure upon the thorax, and passive movement of the limbs or trunk (Rosenthal's method). Active exercises include the combined arm and respiratory movements first practised by Lind and recommended by Knopf and Lagrange, cane exercises (Lubit), the use of the spirometer, of blowing tubes, inspiration through a partially closed glottis (Fischer), the use of inhalations, etc. More recently Kuhn has devised an aspiration mask, which retards the inspiration through the nose to any degree. Expiration is made through the mouth. By this means a state of passive hyperæmia of the lungs (Bier's treatment) ensues, as well as strengthening of the inspiratory muscles.

The simplest form of respiratory exercise is sighing. It can be practised freely without danger every five or six paces while walking or every few minutes while at rest. Walking up gradual inclines accomplishes the same end. Singing also requires deep breathing and to some may prove injurious. Only those patients with normal temperature, pulse under 100, with incipient or moderately advanced, localized, or slightly disseminated, inactive pulmonary lesions, should be subjected to pulmonary exercises. Active or multiple cavities, old or advanced fibrosis, severe laryngeal involvement and hæmoptysis, as well as dyspnœa and palpitation after the exercises, are contra-indications. In fact, there is no reason to believe that the majority of patients do not breathe deeply enough, and for these such exercises are unnecessary. Pulmonary gymnastics have never been practised at the Adirondack Cottage Sanitarium, and the results do not indicate their omission.

**Dietetic.**—One can almost say that correct nourishment in far-advanced phthisis is of greater importance than fresh air (Dettweiler) and in all stages it is of at least equal importance. The main object of dietetic treatment is to enable the patient to regain his lost weight, but not to make him a "flabby, breathless mass of inert fat." A patient who eats and digests well is a patient half-cured (Petit). The powers of assimilation are greatly increased by life in the open air. The teeth should receive careful attention and be placed in order at once.

The preparation and serving of meals should receive the strictest attention, as the kitchen is the only pharmacy that many patients should know. The meals should be carefully chosen and each planned in relation to the preceding. The physician should carefully scrutinize the diet and lay down

broad general rules. It is a wise plan to vary the articles of diet as much as possible and special dishes on special days of the week should be avoided when possible. The table should be attractively arranged and the food well and quickly served (not quickly eaten). Many patients will eat well if the courses follow one another in rapid succession, whereas if long delays occur, cough or fatigue may prevent the eating of the desired amount. To pile up a plate with large amounts (as is done in Germany), and to expect a patient, who especially at first has little or no desire for food, to consume it is a mistake. Repeated helpings until the desired amount is eaten is preferable.

In all acute and subfebrile cases the meals should be served in the bed-room or on the veranda, and when possible a nurse or attendant should be constantly present to supply any wish or whim of the patient and to encourage, to coax, or even to command him to further effort. As convalescence is established the patient should be allowed to come to the table for one meal a day, usually the midday meal. Congenial table companions are almost a necessity in order to obtain the best results.

Much diversity of opinion exists about the regulation of meal times and lunches. Good results can be obtained in a variety of ways, but it is wisest to conform as nearly as possible to the previous habits of the patient. Flick obtains excellent results with one meal a day (a generous dinner) and milk (2 or 3 glasses) and 2 eggs with a little bread, butter, and cereal at breakfast and supper. Lunches of milk and egg are also used, but nothing is given for four hours before dinner. In all 3 quarts of milk and 6 eggs is the daily allowance. The usual treatment, varying slightly for the different parts of the world, consists of three meals and three lunches a day, alternating usually in America, at 8, 10.30 A.M., 1, 3.30, 6, and 9 P.M. The lunches may consist of eggs, milk (hot or cold), beef juice, koumyss, kefir, broth, or some prepared food. When the true normal weight is attained, the lunches may be dispensed with unless the patient feels the need of them. It is often advisable to omit the lunches one day in seven, usually on Sunday, when some extra dishes are usually prepared. In brief the patient should not know hunger, but neither should he be deprived of the pleasures of an appetite (Prioleau).

The following dietary is the one frequently followed, and gives on the whole excellent results: A glass of milk is given before rising, which may be hot if desired and contain a teaspoonful of whisky if the cough is severe and distressing. Beef juice may replace the milk. Breakfast, served at 8 A.M., should consist of fruit, cereal and cream or butter, eggs, steak or chops, with a little broiled bacon, bread and considerable butter, one or two glasses of milk, and a cup of tea or coffee. If deemed advisable a glass of milk or a raw egg should be taken at 10 to 10.30 A.M. Dinner at 1 P.M. should consist of soup, or tasty bouillon or broth, fish or oysters, rare roast beef, mutton, turkey, chicken, and occasionally for a change, if desired, ham, pork, duck, or a little goose; fresh vegetables in abundance and variety; salads with an oil dressing, puddings, jellies, or ice-cream, simple cake. One or two glasses of milk may be taken at the end of the meal and bread and butter in abundance. A demi-tasse of coffee is permissible. All sauces should be prepared with good butter. When prescribed a glass of milk or an egg may be taken at 3.30 P.M. Supper at 6 to 7 P.M. should include cold roast beef, mutton, chicken, occasionally ham, or eggs; a hot meat with vegetables is often very agreeable; bread, butter, tea, cocoa, milk (one or two glasses),

jam or fruit (fresh or preserved). A glass of milk at bedtime and another during the night if awake may be given in some cases.

The amount necessary for an individual is difficult to determine. Every patient should be told that he must eat to recover. He may not experience real hunger, but an eating appetite, an appetite that increases as one begins to eat, one which enables him routinely to eat all that he should, is to be most highly prized. When first subjected to treatment the appetite furnishes no index to the state of the stomach or the powers of absorption. All forced feeding should be controlled by examination of the stools for undigested food. Patients who have reached their highest known weight, if it corresponds to the normal weight for age and height, those with chronic fibroid pulmonitis and impeded circulation, those with enfeebled hearts, those with acute processes and very high fever, those whose failure of appetite and digestion is in excess of that caused by the general constitutional weakness, all these should not necessarily enlarge their diet (Burton-Fanning). Many patients chronically overeat, and in a few overeating becomes a fixed idea. Too much is as bad as too little food. In general it may be stated that a patient should consume as little food as is necessary to enable him to gain on an average one to two pounds per week until his normal weight is attained. When the true normal weight is reached the diet should be slowly reduced and the lunches gradually abandoned, if the increase of weight coincides with an arrest of the lesion. Proteid excess, especially, should be carefully avoided, while excess of fat is well borne.

Debove's method of suralimentation, filling the stomach with a mixture of chopped meat, eggs and milk, yields permanent success in few cases. Good results, however, have been obtained by v. Ruck.

Patients with slight fever can usually digest easily all good, plain, wholesome, solid food. Those with high fever may have some difficulty and should receive at first a fluid or semifluid diet and solids be added one by one. It is remarkable to see what foods and the amount that can be digested by some patients with persistent high pyrexia. In a few patients the careful use of antipyretics may increase the gastric secretions (Hildebrand) and often enables the patient to eat a good meal. The principal meal of the day should be taken, when possible, during the afebrile period. When the temperature exceeds 102° most patients lose weight regardless of modification of the diet.

Suraliments, any articles of food given in excess of the bodily needs, should be easily digested and assimilated, stimulating, capable of being taken in large enough doses and during a longer or shorter period without disgust, or, better still, with relish, and lastly should not be prone to cause intestinal fermentation or to give rise to toxic action on the liver or kidneys. Among these may be mentioned eggs, milk and its derivatives, meat juice, many fats, and prepared foods.

Milk, eggs, and meat are the most important. It is difficult to overestimate the value of milk, which often enables a patient to regain quickly his lost weight. The amount required varies and in a few large quantities can be taken with little or no influence on the nutrition. From 2 pints to 4 or more quarts are advised by different authorities, but 3 or 4 pints for patients on a general diet is a very good average. A tumblerful should be taken slowly, eaten rather than drunk, with or at the end of a meal and one between meals. Some patients with a strong antipathy to milk, by urging and after a fair trial,

often overcome it. Small quantities should be used at first in such cases. When hot or cold milk is not well borne it may be treated in various ways. A pinch of table salt or sodium citrate may render the milk clot less firm and more digestible. One or more tablespoonfuls of lime-water, the addition of an aërated water, of a little coffee, tea, or even cognac, may enable a patient to take a sufficient quantity. When these fail the milk should be peptonized and taken hot or cold. Koumyss or kefir, possibly with the addition of the *Bacillus lactis aërogenes*, may be tried in case of intestinal fermentation. A considerable quantity of milk may be taken in puddings, junket, porridge, etc. Whey and buttermilk are much less valuable.

Great care should be exercised in procuring milk as pure as possible, for only in this way can some patients take milk and avoid increased pulse rate, fermentation, and diarrhœa. The recent work of Calmette and others has shown that dead tubercle bacilli are not innocuous to patients with pulmonary tuberculosis, and boiling, therefore, does not render milk containing tubercle bacilli harmless. For all these reasons it is a wise plan to know thoroughly the source of the milk, or to use only certified milk. When milk cannot be taken, the amount of butter and cream may be increased or olive oil added to the diet. A little cheese is of value.

Eggs should be strictly fresh; 2 or 3 up to 30 a day have been advised, but for most patients 6 is a safe limit. They can be taken raw, as most prefer, or cooked. In some patients the yolk of the egg causes gastric distress or even purging; these should take only the white.

Meat is of equal importance and it should at first be eaten at three meals. Beef and mutton are to be preferred, and, while the latter is more readily digested, the former proves from experience the better food. Chicken and turkey, while of less value, are better than duck, goose, or fish. Twice-cooked meat should be avoided. Rare meat is better than well-done, and raw meat is held by some as the best, combining the maximum of useful results with the minimum of digestive effort. Raw meat (beef) may be given as scraped-beef sandwiches or in little balls, rolled in chocolate, where the taste is disagreeable, as it needs no mastication. The muscle plasma, ordinarily called beef juice, expressed from meat, raw or slightly and superficially heated (until gray on outside) in a dry saucepan, is of considerable value. The meat should be as fresh as possible, and often the cheapest and toughest cuts (brisket, rump, etc.) yield the most juice. Richet and Hericourt, who first popularized the use of raw meat and its juice (good, though less valuable) under the name of Zomotherapy, advise that the meat be left in a small quantity of water (one-fifth by weight of meat) for two hours, then expressed and the juice (from 500 to 3000 cc.) be immediately taken. Slightly heating the meat increases the amount of beef juice, affects it very little, renders it more palatable, and permits it to be kept throughout the day. Many of the meat powders, containing three or four times as much nourishment as a similar quantity of meat, and easily digested, are unpalatable. Blood, once held in high esteem, is now little used on account of the repugnance many patients have to it. Meat extracts, bouillon, and meat broth, though containing little nourishment, often stimulate a flagging appetite.

**Fats.**—These are of great importance to the tuberculous. Hutchinson has affirmed that by a study of the amount of fat eaten, it could be determined which members of a family would succumb to tuberculosis.

The best form in which to administer fat is undoubtedly milk and its derivatives, butter and cream. Cod-liver oil is much less used than formerly and many patients cannot take it. Combined with malt, aromatic oils, or bitter tinctures it is more palatable. It should never be given during warm weather nor when high pyrexia is present. There is no objection to a good emulsion whose formula is known. Olive oil, well taken by some patients, is valuable. Many fishes contain much oil, *e. g.*, sardines and salmon. The stools should be examined whenever fats are administered, to prevent excess of administration.

Water should be taken freely (1 to 2 quarts daily) between, or preferably hot and one hour before meals. Too much water with the meals may cause flatulence and digestive trouble. Coffee, tea, and cocoa may stimulate the organs to take up more nourishment.

Many prepared foods have been used with apparent success. They should fulfil the requirements of a suraliment. Animal food rich in nitrogen is poor in phosphorus and vegetables supply this deficit. Vegetable juice, recently suggested by Russell, has not yet been proved of much value. Fruits and nuts are of value and the grape cure in France has been recommended.

**Institutional Treatment.**—To institutional treatment the proof that pulmonary tuberculosis is curable is largely due. For many years the sanatorium was looked upon as the central point in the struggle against tuberculosis, but more recently it has become evident that only a small fraction (possibly not over one-tenth) of the tuberculous patients could gain admission or leave home to undergo treatment at these institutions. Today institutional treatment may be said to centre about the dispensary, which selects patients suitable for the sanatorium or hospital and treats the remainder scientifically and with excellent results.

**Hospitals.**—The hospital, of great value in prophylaxis, is of less aid in treatment, which in most general hospitals is, as Bernheim says insufficient, illusory, and dangerous both to the tuberculous and other patients.

**Dispensaries.**—The dispensary, the most potent factor in the struggle against tuberculosis, affords at the present time the best treatment for those patients (almost 80 per cent. of all) who, still able to work, must do so and remain at home. It should coöperate with all existing charities, should be open early in the morning, in the evening, and at some time on Sunday for working patients. The trained nurse, who should possess tact, energy, interest, and ability, is indispensable. She visits the home of every new patient, makes a careful detailed report of the social condition, and revisits old patients to see that the instructions are properly carried out.

**The Sanatorium.**—*Historical.*—The application of the sanatorium treatment, originated by Brehmer, in 1859, spread slowly for some years, fostered by the originator, Dettweiler, Turban, and a few others in Europe and by Trudeau and later by Bowditch, in America. To America belongs the honor of establishing the first sanatorium for the needy, the Adirondack Cottage Sanitarium, founded in 1884, by Trudeau, who by his marvellous enthusiasm has almost single handed year after year raised by private contributions the deficit of this institution, now amounting to $25,000 per year. Following in the footsteps of Dettweiler, V. Y. Bowditch, of Boston, founded the first sanatorium in America in a "home climate," and opened the way by his splendid results and his own efforts for the establishment of the first State sanatorium (Massachusetts, at Rutland).

The objects of the sanatorium are twofold, healing and educational. In Germany the insurance sanatoriums and those for the poor aim more to restore the working capacity than to arrest or to cure the disease. The sanatorium should aim to arrest every patient, and, if possible, to do so in a period of residence of six to twelve months. However, many cannot be brought to arrest, much less to apparent cure, but for these patients the educational influence is of great value and many ultimately recover by means of the knowledge so acquired. On leaving the sanatorium they teach how to prevent infection and still foolish alarms.

*Advantages.*—While at the sanatorium the patients are under more or less constant supervision in regard to every detail of their lives; the companionship of "fellows in distress" soon overcomes any feelings of restraint or of homesickness, and habits of passive resistance are easily put aside. Many patients, especially those in pleasure resorts, foolishly keep up a pretence of well being, which in a sanatorium, where all is conducted on the basis of ill-health, is never attempted. The close supervision of diet, of rest, and of exercise for one or two months at the beginning of treatment is probably the chief advantage of the sanatorium.

*Selection of Patients.*—This is most difficult in some instances and depends mainly upon the prognosis. Patients under fifteen years of age should be in special institutions with educational advantages, and those much beyond fifty rarely fully recover. In general all patients with incipient disease, and many in moderately advanced stages, are suitable for sanatorium treatment. Far-advanced or hopeless cases should not be admitted. Patients with tuberculous complications, or with albuminuria, diabetes, a persistent diazo reaction, chronic diarrhœa, melancholia, profound neurasthenia, or pregnancy, are not acceptable. Patients with slight tuberculous complications, such as slight thickening in the posterior interarytenoid space, slight superficial ulceration of one cord without infiltration, fistula-in-ano, often do well. Former patients who have relapsed often do badly. Patients with pronounced symptoms out of proportion to the physical signs, with marked, persistent tachycardia or pyrexia (at home and at rest), those who have steadily declined since onset, with continuous loss of weight in spite of hyperalimentation and those with marked dyspnœa on slight exertion are not suitable.

The older the lesion, when slight, the less likelihood of an unfavorable result, but the curability of a patient during sanatorium treatment is inversely proportional to the duration of the disease. Patients in whom the lesion extends over a greater extent than one lobe should be excluded, as well as all patients with cavity. The most favorable cases are those with a few rales at one apex with or without catarrhal symptoms. The involvement of both apices, with a few rales extending to the level of the second rib and third vertebral spine, without dulness or marked respiratory change, are less favorable, but suitable. Patients with more extensive physical signs, due to pleurisy, are also favorable. The admission of a patient with four to eight children, whose wealth is his ability to work, entails serious problems. The family must be provided for and suitable work arranged for him on discharge, otherwise he is not a fit subject in one sense for sanatorium treatment. Extreme poverty places a patient's ultimate recovery in grave doubt.

For institutions which are anxious to obtain good results, the only safe plan is to have a large waiting list, to keep each patient some weeks under observation or to select the most suitable from the list, a practice which works

much hardship upon the patients, and is not to be recommended. The sanatorium should endeavor to exclude all non-tuberculous patients and every patient in whose sputum tubercle bacilli are not or have not been found should be subjected to the tuberculin test.

*Treatment.*—The treatment of patients in a sanatorium must be individualized and "hospitalization" avoided. Firmness, not dogmatism, should be aimed at in connection with all rules, as well as great common sense. The patients act in many instances like children, and the responsibility that rests upon the shoulders of a true sanatorium physician is not light nor easily borne. Many factors are discussed elsewhere and the following paragraphs refer mainly to afebrile patients, able to be up and about.

*The Daily Life.*—On admission the patient should spend at least two weeks in the infirmary or reception cottage, where he is under close and constant observation and is taught many things that usually require months to learn at home. It is a grave mistake so to watch over the patient that he feels he need no longer consider whether an act is "right or wrong" for him. This weakening of self-control may result disastrously when the patient returns to his former surroundings, and is in a certain sense one of the objections to sanatoriums and a great argument for home treatment.

Strict rules are very necessary, but should be as few and simple as possible. Smoking at stated intervals for selected patients may be indulged in, but only out-of-doors, and inhaling should be forbidden. All patients should be required to be in bed with lights out at from 9 to 10 P.M.

Visitors should not be allowed to interfere with the daily routine, but at some time during each patient's stay at the sanatorium some member of his family should visit him to see what he should do on returning home. Provision should be made for only one or two visitors at any one time. No visitors suffering from colds or influenza should be admitted.

*Amusements, Classes, Work.*—In all sanatoriums the time passes slowly for many patients and every opportunity to encourage idleness is afforded. This tendency should be strongly combated by suitable work, classes, or amusements. A good library with the current magazines, and a piano for those patients who are allowed to play, are important. Photography and sketching are useful, but nature study is far more valuable than any of these. To arouse or instil a love of birds, flowers, geology or some kindred subject, an interest which the patient will carry with him through life wherever he goes, is of extreme value. Every patient if possible should leave the sanatorium with an outdoor hobby. For many nature study has no charms, and for these arts and crafts of wide variety should be provided. Lectures should be given at intervals upon hygiene, and any subject of interest.

Suitable useful work at the sanatorium is a great mental relief to many patients who envy the man who is allowed to do most. It also fits many to return to their former occupations, which must frequently take place.

Work at a sanatorium depends much upon the class of patients accepted. The laboring man who has used his muscles can safely attempt work which would be injurious to the clerk or stenographer. Many charitable or semi-charitable sanatoriums require all patients to do some work, which, however, should be done leisurely and never under tension. For men this is usually some form of gardening, but at the White Haven Sanatorium, under Flick, the patients have long done practically the entire work of the institution.

It is needless to say that patients at work need very careful medical super-

vision, and malingerers often have to be overlooked for fear of injuring an honest patient. Ample time for rest should be afforded.

*Length of Stay.*—This varies from an average of three months in the insurance sanatoriums to one to three years in some private institutions. No permanent benefit to the lungs can be hoped for in less than three months, and when the disease has passed its veriest incipiency a "cure" should not be expected in less than two or three years. In fact, more patients require four or five years to attain a cure. For those dependent for their livelihood upon their own exertions, six to twelve months should be an average length of stay, but on discharge the patient should be frankly told that the next two years are the most dangerous for him. If he return to work, he must work and take care of himself, and he cannot usually play as well.

In some instances it is very difficult to decide when a patient should leave the sanatorium. As long as occasional attacks of fever, a persistently rapid pulse, and fatigue after slight exercise are present, the patient's position is still insecure. When, however, the patient can work or take considerable exercise, needs no longer a forced diet to maintain his weight, has been apparently well for three or four months, he may safely consider returning to his home and leading a similar life until fitted to resume work.

*Modifications.*—It has long been recognized that a large number of patients must remain at home, usually in crowded quarters of cities, and many schemes have been employed to aid these. Day sanatoriums, including the "classes" of Pratt and the camps of the Boston Antituberculosis Association, where patients are instructed and given facilities for pursuing treatment have met with great success. The night sanatorium, where patients who must work can sleep out-of-doors, is another valuable addition.

**Home Treatment.**—The immense majority of all tuberculous patients (98 per cent.) have to be treated at home. At least 75 per cent. of those who seek "sanatorium" or climatic treatment return to their homes long before the disease is cured or even arrested. Only a small fraction of 1 per cent. of all patients remain permanently in a different climate and do not at some period pursue their treatment at home. This may be defined as treatment in the land in which the patient lives and contracted the disease, be the elevation high or low. It may be carried out either in the home of the patient or in a sanatorium. The treatment pursued in many of the "open" health resorts is, for those who can afford it, treatment in their homes, and many of the objections urged against home treatment apply to this.

The value of home treatment cannot be questioned. Patients in early stages do well in any climate. The statistics of sanatoriums in the "home climate" show excellent results, but few figures are available for a study of the results obtained outside of sanatoriums.

Treatment at home is less expensive, does not entail residence in a hotel or boarding-house or acclimatization after return to work; precludes separation from the family and friends, fatigue of travel, homesickness; does not break up business arrangements in the same degree, and in fact possesses every advantage, according to Flick, but climate. Further, "at present instead of finding the best trained experts for the treatment of tuberculosis in health resorts, with some notable exceptions, we find them in the large centres of population; and the opportunities for getting expert treatment are perhaps better in large cities than in some of the health resorts" (Flick). The gain in weight is often very rapid at home.

A most important factor is the training of the family. They too must adjust their life to the needs of the patient, must shield him from worries and care, must encourage him in his hard struggle, and should be made to fully realize the length of time required. When this is once accomplished the adjustment of the future life is more readily obtained, more consideration is afforded both by friends and by the family, and permanency of the results is better assured.

It requires more moral stamina to sit out alone in a damp, cloudy, foggy climate than to do so surrounded by pleasant companions in a bright climate. The care and worries of home life are never fully lost. The mother cannot neglect her children nor can a merchant calmly neglect his business. The anxiety produced by sickness cannot be avoided at home. A selfish, exacting family is an indication for a change of residence and no patient who has long borne all the burden of the family should be allowed to remain at home. These disadvantages of home treatment are neither few nor slight, but, once met and overcome, the permanency of the results is at least theoretically better.

There are four classes for whom home treatment is especially advisable—patients in far-advanced stages; the desperately poor; those whose income ceases when they stop work, but who can for a while, at least, have good food and rest at home; those who for domestic and other reasons (antipathy to change of climate) will take their chances at home (Otis).

When possible the patient should move to the healthiest locality in the region. A change to the country or at least into the suburbs for a year is advisable. The house should stand well back from the street and not too near the neighboring houses, should have a sunny exposure, and, if possible, be at an elevation of 300 to 700 feet. The neighborhood of factories, gas-houses, power-houses, etc., should be avoided. A sunny room, 12 x 14 feet or larger, with a ceiling 10 feet high, lighted by electricity, heated with hot water or steam, with two windows, or a window and a door opening out on a sunny balcony protected on one side with glass on which the bed may be rolled, makes an ideal place. These conditions, however, can rarely all be obtained, and many shifts for the "cure" must be made. A tent in the back yard or on the roof, a bay window or even a well-ventilated room may have to suffice for a time. The question in the tenement-house districts is more difficult. The dispensary, with its distribution of foodstuffs and its visiting nurses, is of vast importance. The problem of good food with the poor is more serious than that of fresh air. Fairly good results have been obtained by placing patients on farms. A few weeks' residence at a sanatorium or the services of a trained nurse well versed in the treatment of pulmonary tuberculosis for a few weeks is of much importance. The care of the patient and of his room should approximate as closely as possible to that employed in a sanatorium. The patient should always have a bed to himself.

**Climatic Treatment.**—The value of certain climates has in recent years been called into question and today rests largely upon personal belief and experience. Much has been written and little proved. There are localities differing widely in every climatic element in which man does well—why, we often cannot say. The advocates of climatic treatment include many men in and outside of health resorts. "Every man," says Sandwith, "who lives in a health resort becomes early inoculated with the microbe—I do

not know its Latin name—but it means the microbe of universal belief in the place in which he lives." The opponents include a few men who have lived in such localities, but the majority base their opposition on the good results obtained at home and on observations in health resorts usually of short duration. Many climates unquestionably exert some influence upon man in health.

There is no specific climate for pulmonary tuberculosis, and a good climate alone is of little avail. Many believe that residence in a health resort hastens improvement or deterioration. Without doubt many of the effects attributed to climate can be ascribed to change of climate. Change from a "good" to a "bad" climate often produces excellent results. "The air of any place," said Cullen, "is better for a patient than that in which he grew ill." Too frequent change of climate, a *Wanderlust*, may, however, result disastrously. It is rarely advisable for a patient to remain in any climate without change for more than eight or nine months. Some need more frequent changes, which can often be accomplished by a change of residence in the same locality.

The objects of climatic treatment are to furnish a complete change of environment, to withdraw the patient from the influences under which he contracted the disease, to subject him to a climate which will promote healing in the lungs, by increasing the activity of the digestive functions and thus stimulating nutrition, by improving the tone of the nervous and circulatory systems, either by invigoration or protection, and by lessening the exposure to secondary infections. Further, and of no less importance, climatic treatment may have for its object palliation of distressing symptoms in patients whose disease may not prove fatal for months.

The ideal place for a patient with pulmonary tuberculosis should possess purity of air, a dry, porous, salubrious soil, good potable water in sufficient quantities, good sewage disposal, relative protection from wind, and such a temperature that the patient can spend hours out-of-doors without discomfort. Abundant sunshine, infrequence of fogs, the persistence of snow, if it occur, throughout the winter, are all of value.

The purity of the air varies inversely with the density of population, which varies with the altitude, the precipitation, and industrial opportunities. The purest air is found over the ocean, in the interior of deserts, and on mountain peaks. Traffic creates dust. Low humidity, usually coincident with scanty precipitation and little or no vegetation, is productive of much dust. The desert climates, the high plateaus east of the Rocky Mountains (Colorado, New Mexico, Wyoming, and Arizona), all suffer from dust and sand storms, greatly irritating to sensitive mucous membranes of the upper respiratory tract. One of the great advantages of snow is that it prevents dust.

Wind has been described as an etiological factor in pulmonary tuberculosis, but its chief action is, no doubt, due to keeping the population indoors where with all crevices carefully closed the ventilation is poor. In cold climates the sensible temperature is greatly reduced in the wind and in all climates patients should be able to obtain full protection from it. It greatly purifies the atmosphere, although in excessively dry climates it creates much dust. Forests and vegetation prevent dust, protect against wind, and render the climate slightly more equable.

The temperature of the climate must be carefully considered in each

individual case. The fundamental point in the selection of climate is, Huggard holds, its action on the tissue change, which depends on its heat-abstracting powers, which in turn depend upon the temperature in combination with the humidity and wind. Heat demands may be large or small, regular or irregular. In warm climates these demands depend chiefly upon the moisture, while in cold climates wind determines them, as air nearly constantly below 30° is always, at least for therapeutical purposes, dry. The best climate for any patient is one where the demands for tissue change best coincide with the patient's powers of response. It is this factor which determines for any individual whether a climate is bracing, relaxing, or depressing. These powers of response can never be accurately foretold, but careful inquiry whether the patient does better as a rule in winter or in summer, how he withstands cold and heat, the state of the muscular system, of the skin, and of the organic functions, will often enable a fairly accurate forecast to be made.

Young persons usually meet high heat demands well, those past fifty years more uncertainly, while older individuals fail to meet them. Younger, fairly robust or robust patients, therefore, demand a climate of invigoration, which is cold, dry, variable (a diurnal variation of 20°) and more or less elevated, while older, more or less delicate persons need most frequently a climate of protection which is warm, moderately dry, equable, sheltered, and lying usually at much lower levels. Large eaters, often somnolent in summer, usually stand cold well. Patients susceptible to chilblains, and to Raynaud's disease, may do remarkably well in cold climates. Patients with pulmonary tuberculosis often do best in a climate with low humidity and with moderately low or low temperature, but a few are better suited with high humidity and high temperature.

Symptoms have long been used as a guide in the choice of climate. The increase of cough and even of expectoration that occurs on change to a cold climate was long advanced as an argument against cold. More recently it has been clearly recognized that the increased nutrition amply offsets this exacerbation of cough, which in patients suitable for such climates soon ceases. A dry climate is suitable for free secretion and a sea climate for scanty secretion in bronchitis, but the same does not necessarily hold in pulmonary tuberculosis (Lindsay). A tendency to hæmoptysis need not be considered unless in a patient with extensive cavities, when high altitudes are contra-indicated. It is wise in any instance to postpone travelling for at least two weeks after hæmoptysis. Patients with chronic catarrh should avoid windy places (Weber); those with asthma should go to moderately elevated localities if young, to warm resorts with slight elevation if older.

Acute pulmonary tuberculosis is a contra-indication to change of climate. A temperature of 99° to 100° in the morning, rising to 101° to 102° in the evening, precludes travelling. When the temperature falls to normal in the morning a change may be considered. Persistent tuberculous diarrhœa, extensive laryngeal invasion, pneumothorax, advanced nephritis, marked dyspnœa with cyanosis, cachexia, and grave diabetes are complications that usually contra-indicate change of climate, although life in many cases may be prolonged and suffering alleviated by change from a colder to a warmer clime. It should never be advised unless the patient can obtain every comfort. In general, patients in acute stages should be kept at home. Robust

patients in subacute stages, or with chronic ulcerative disease, within certain limitations, may be sent to any climate. Patients with advanced fibroid disease, delicate patients with subacute or chronic ulcerative disease, need a climate of protection, neither too cold nor too high, but those in early stages will do well in almost any climate.

The mental characteristics, habits, and surroundings of the patient at home must be considered. The pecuniary condition is of much importance. No patient should seek health in an open resort without $250 or sufficient for a six months' residence besides his railroad fare. The opportunities for work at health resorts are slight, as the field is already overcrowded. The practice of sending patients to health resorts with the advice to live out-of-doors, to exercise freely, and to consult no physician is criminal. It is inexcusable to send patients to places of which the physician knows little or nothing either in regard to the expense, the accommodations, or the medical fraternity. A few wise, frank words of good medical advice *on arrival* may prevent a serious relapse or fatal illness. Great caution should be exercised for the first two or three weeks in a new climate. "Fashionable" resorts should be tabooed during the "season." Resorts that frankly acknowledge "tuberculosis" and take suitable precautions are much safer than those in which tuberculous patients are designated as "bronchitic" or "nervous."

**Deserts.**—The chief characteristics of a desert climate may be said to be purity of air (considerable ozone), dryness, a maximum amount of sunshine (and of light), great but constant variations of temperature between day and night, and slight precipitation resulting in few cloudy days, lack of vegetation, and much dust. The continuous sunshine and the lack of vegetation are very trying to a few patients, but the majority take great delight in the absence of cloudy, depressing weather. Many patients with advanced disease are sent to desert regions, which explains the fact that very weak patients are said to grow weaker, that hæmoptysis, if severe, becomes worse, and no doubt explains the fact that C. T. Williams has seldom seen an arrest in the desert.

The following indications for desert treatment may be of aid: (1) Pulmonary lesions complicated with nephritis, with frequent bronchitic attacks, or with rheumatism; (2) patients advanced in years; (3) those with advanced lesions, who endure cold badly and cannot live at high elevations. Among the contra-indications are dry catarrh of the upper air passages, marked laryngeal inflammation, intestinal disturbances, while some authorities mention also heart disease, hæmoptysis, and weakness. The best-known desert climate is that of Egypt, which entails a long trip and much expense. Cairo should be avoided and the patient should go at once to Mena House, Helouan, Luxor, or Assouan. Weber opposes the Nile trip. The oasis Biskra in Algeria has been recommended. The United States, however, possesses the most varied desert climate with an elevation varying from sea level to 6000 feet above. Vast areas in Arizona, New Mexico, Utah, Southern California, and Colorado possess all the characteristics of a desert climate.

**Marine Climates.**—A marine climate is characterized by purity of air, an equable temperature, high humidity, high barometric pressure, great luminosity, and complete absence of dust and bacteria. Some tuberculous patients are very refractory to the influences of the sea climate, but for the majority the marine climate may be said to be sedative as well as tonic.

The indications for a marine climate include anæmic, nervous patients, susceptible to cold, with glandular complication, bronchial catarrh, emphysema following fibrosis, and heart disease. Sea bathing is not advisable, but douches and sponging with sea-water may be employed.

The most famous marine climates are those of the Riviera and of Madeira. Long employed for all patients, they have in recent years been more closely restricted to far-advanced patients and for those not able to stand colder climates. In America the coast climates are employed more frequently during the summer.

Sea voyages were formerly much recommended, but in recent years have fallen, and for the majority of patients justly so, into disuse. The position of ship's surgeon for a tuberculous physician ought to be recommended only under the most favorable conditions.

**High Altitudes.**—"High altitudes" may be said, at least for therapeutic purposes, to begin at 4000 feet elevation, while those above 7000 feet need little consideration. The configuration of the local region, the direction of the mountain ranges, the north or south side of the range, the side facing the prevailing winds, the proximity to water, forests, etc., all affect the climate of resorts in high altitudes.

The characteristics of these are low barometric pressure with consequent reduction of oxygen, purity of air, low humidity, much sunshine of great intensity, a soil usually dry and porous, and great difference between the temperature in sunshine and shade. The amount of wind, usually large, varies greatly for different resorts in the same region, while the amount of snow is more or less closely associated with the latitude. The temperature in winter is usually low and the heat never oppressive in summer. The effect of these factors upon the human organism has long been studied and the results of this research are very variable and in many instances contradictory. The thorax in time becomes larger (1 to 3 inches) and more mobile, depending on age, and to some extent upon exercise. Some increase of pulmonary ventilation persists for four months after a return to low elevations. Nutrition is stimulated and the increased oxidation takes place at the cost of the carbohydrates, with a consequent lessening of the fatty tissue. The appetite and weight are usually increased. The nervous system is strongly affected; a feeling of greater endurance and of great stimulation is noted at first, and less sleep is required. Marked nervousness at times results.

The low barometric pressure produces some stasis in the peripheral circulation and a change in the distribution of the blood. The pulse at first and for many months in some is quickened and the increase after exercise is more noticeable than at lower levels. At first palpitation may occur and the blood pressure be lowered. The effect upon the blood has not yet been finally settled, but an increase in the number of erythrocytes in the peripheral circulation takes place at the rate of about 50,000 for each 1000 feet of ascent. During the first few weeks (usually three) at high levels the erythrocytes gradually decrease, but later a real increase, as well as a more rapid proliferation of the red bone-marrow, has been noted. In some anæmic individuals the number later never falls below normal.

The effect of high altitudes upon patients with pulmonary tuberculosis is difficult in many cases to foresee. It is harder for them to become acclimated, and some may never do so. Great caution in regard to rest, exercise,

and food should be practised for four or five weeks. Medical advice on arrival in a high altitude is of the utmost importance. Hæmoptysis does not occur more frequently in early stages. The chill resulting from change from sunshine to shade or at the setting of the sun should be carefully avoided. The duration of the treatment varies directly with the condition of the patient, but most authorities state six months as a minimum. Lauth believes that in a few months all the possible benefits are acquired and a change to a lower elevation, followed by a return to the high level, will produce better and quicker results. The winter season is usually believed to produce better results than the summer, although little proof of it exists. In regions where snow persists throughout the winter, patients are often advised to leave before it melts. It is now recognized by many authorities that no change should be made until the weather is settled at the locality to which the patient journeys. Many patients after recovery return from high levels to low with no ill results, but some find they must reside permanently at a considerable elevation. There are four reasons why a patient should go to a lower elevation: lack of improvement, cyanosis, and difficulty with sleep or breathing (Bullock).

The indications for treatment in high altitudes are far from exact. The general condition is of great importance, and a constitution capable of some resistance and organs capable of increased nutritive and oxidizing work are necessary. If the foregoing conditions be not fulfilled, or if albuminuria, severe diabetes, pronounced emphysema, grave anæmia, nervousness, rheumatism, or severe gout be present the patient should not seek health in high altitudes. Marked arteriosclerosis, cardiac dilatation (unless very slight), nervous derangements, persistent tachycardia, pronounced aortic or mitral regurgitation uncomplicated or complicated by pleural and pericardial adhesions, forbid this treatment. Patients with feeble circulation, great susceptibility to cold, tendency to fever with slight ailments (erethic constitution), with small lung capacity (although little damaged), with a strong tendency to alcoholism, with marked tuberculous nephritis, or with organic disease of the brain and cord, are not suitable. Cavity formation with a tendency to hæmoptysis, an age of fifty years or over, are contra-indications. Some hold slight urogenital tuberculosis, severe anæmia, or severe neurasthenia in pulmonary patients as doubtful indications for high elevations.

The most famous resorts in high altitudes are the Alps, the Rocky Mountains, and the Andes. The last is little used for patients in the northern hemisphere. The Alps are colder, have much more snow, more precipitation, more vegetation, are more frequented by healthy individuals, but offer much less opportunity for future employment than the Rockies. The latter are more suitable for weaker patients, have more sunshine, more wind, and more dust. Suitable accommodations are less expensive in the Rockies. Smelting towns should be avoided.

Many health resorts lie at a moderate altitude (1000 to 3500 feet), and it is still unsettled at what elevation the physiological phenomena attributed to this factor are first apparent. They cannot be said to have any peculiarly characteristic climate, but vary according to their latitude, or to their proximity to sea or desert. The only feature they have in common may be said to be purity of atmosphere. The best known of these resorts in America are the Adirondack Mountains, the regions about Asheville, about Liberty (N. Y.), parts of Maine, the Muskoka region, St. Agathe, Quebec, etc.

**Balneotherapy.**—The effect of balneotherapy upon pulmonary tuberculosis has long been questioned. The climate of many of the spas found of avail in this disease, is often mountainous and excellent, but the duration of the treatment, three to six weeks, is too short for such a chronic disease. The value of this treatment may be said to be purely symptomatic, and closely similar results can often be obtained by other means. The large quantity of water taken is, however, of considerable value. Advanced, febrile, cachectic patients and those with a tendency to hæmoptysis should not take the water at a spa. The slight intoxication from mineral waters containing carbon dioxide must be carefully avoided. The waters of saline springs are of value in the catarrh of quiescent, torpid, and anæmic patients.

**Post-discharge Treatment.**—The treatment of pulmonary tuberculosis is a question of years. A residence of some months in a sanatorium, in a health resort, or at least in the open air away from business, should be insisted upon. On the return to the active duties of life the patient should have made clear to him that the struggle is not over and will not be over for four or five years. On discharge from treatment he should be given a card which contains his proper weight for his height and age, the lowest limit of safety, lists of suitable occupations and sports, brief statements concerning hours of rest (in bed), sleeping out, the normal pulse and temperature range, etc. Following climatic treatment the patient must again become acclimated to his home climate and adjusted to his former surroundings.

For months he should exercise the greatest care and live as nearly as possible the life he has been pursuing. Those who recovered under the home treatment have an advantage in this respect. The many small details should be carefully observed. The cold sponges, eight to ten hours in bed every night (preferably out-of-doors), strict avoidance of all persons suffering from colds and influenza, working only in well-ventilated rooms, avoidance of dust, of cramped positions, of fatiguing occupations, especial care about the diet and bowels, are all matters of great importance. The real value of sleeping out now becomes apparent. Eight to ten hours a day in the open and sleeping in a well-ventilated room are sufficient for most patients, but on return to work in rooms, more or less poorly ventilated, sleeping out becomes almost a *sine qua non* of continued good health. Many devices have been employed to approximate these ends. A few patients find that permanent residence in a good climate is often necessary to enable them to work. The selection and procuring of suitable occupations for working men and women is of vast importance and of great difficulty. Whenever possible the full quota of work should not be attempted at first, but gradually attained. Light work indoors is better than heavy work out-of-doors, and easy work in a home climate is far better than severe work in a health resort.

For the well-to-do the problem is easily solved; for the working man, especially the skilled workman trained to but one small part of a trade, the problem of future work is oftentimes more serious than that of recovery. The agricultural colony should be closely associated with the sanatorium to achieve the best results.

**Symptomatic Treatment.—Fever.**—This coincides in most cases with the treatment of the disease. Every patient should have fully explained to him the ordinary causes of fever, such as excitement and overexertion. He should, further, be told that slight coryza, simple angina, constipation, and diarrhœa may cause fluctuations in his temperature and that a subnor-

mal temperature, when every other symptom is favorable, needs no treatment; that the indications for rest depend not upon the low morning, but upon the afternoon or highest temperature. If fever occurs during the menses the patient should remain at rest, or, better, in bed for the first day or two. A rise of the morning or minimum temperature, even if it does not exceed 99° (oral), indicates absolute rest, and if it reaches 99.5°, rest in bed for several days may prevent a long and stubborn attack. Patients especially prone to fever should avoid heated discussions, and prolonged visits should not be allowed. Exciting games, many visitors, an exciting novel, writing many letters, or attempting to transact business should all be forbidden.

*Rest.*—This has long been adopted as the most efficient method of combating fever in pulmonary tuberculosis. In many instances rest can be enforced only when the patient remains in his room with wide-open windows. To employ rest properly, however, it should always be taken out-of-doors, and a small, well-sheltered porch upon which the bed can be wheeled from the bed-room is ideal. The amount of rest required varies directly with the degree and persistence of the fever. A slight rise of temperature in a patient previously afebrile should always be treated by rest in bed, out-of-doors if possible, when the temperature reaches 100° at any time of the day. A few days' rest in bed will usually suffice to bring the temperature down to normal, but the patient should not be allowed to get up until his temperature has been 99° or lower for three consecutive days. A rise to 99.5° (oral) would contra-indicate all exercise except dressing, although permission may in many cases be given to go to the table for meals.

In some cases it is impossible to get the temperature below 99.5° to 100° every afternoon, even after prolonged rest in bed. If such a patient becomes depressed, loses his appetite, has a poor digestion, and begins to lose the weight previously gained, and if sleeping out at night does not reduce the fever, he should be allowed to sit in a reclining chair on the balcony for half an hour each morning, but should not dress. If this does not raise the temperature the time may be increased, or he may get up in the morning for a short time. Some patients unquestionably improve more rapidly under this treatment, and those with digestive trouble are often helped by this plan. Short walks may assist greatly in the recovery. However, if the minimum temperature is high, *i. e.*, if the temperature is continuous, great care should be exercised. All patients whose temperature reaches 101° or over should be kept in bed for weeks if necessary or until, after a consultation, all hope is abandoned. The results of rest in fever are well shown in the table of Burton-Fanning:

| Average maximum temperature for first week of treatment. | Number of cases. | Percentage in which temperature became normal. | Average number of weeks required to reduce fever. |
|---|---|---|---|
| Between 99.0° and 99.5° . . . . | 37 | 87.5 | 3.6 |
| Between 99.5° and 100.0° . . . . | 18 | 54.4 | 5.7 |
| Between 100.0° and 100.5° . . . . | 11 | 46.6 | 4.8 |
| Between 100.5° and 101.0° . . . . | 9 | 34.2 | 6.5 |
| Between 101.0° and 101.5° . . . . | 6 | 37.5 | 17.5 |

From a study of 716 patients under sanatorium treatment the same author found 50 per cent. lost their fever in an average of one month.

The treatment of acute fever varies with its cause. If due to some non-tuberculous intercurrent disease the treatment usually accorded that disease should be followed, but only within certain limits. If possible the disease should be treated in the open air, and in any case the patient should be put out-of-doors as soon as possible and good ventilation ensured while indoors. If the acute attack is tuberculous in origin the patient should be kept continuously out-of-doors.

*Hydrotherapy.*—This should be employed with great caution and carefully watched. No hydrotherapeutic measures should ever be employed which exhaust the patient, and as a rule only those which do not necessitate moving him should be frequently and continuously used. Sponges, at first with water at 98° and later, when more accustomed to them, with water as low as 50° or 40°, are often refreshing. A salt sponge in the evening, followed by an alcohol rub, refreshes the patient and frequently induces sleep. If the patient is weak, alcohol may be added to the salt-water and not used separately. If the sponges fail to reduce the temperature sufficiently, an ice rub may be given or a cold pack to the trunk employed.

Rectal irrigation with cold water or a water coil on the head or trunk may be used, but are less satisfactory. An ice-bag over the heart frequently quiets the nervous system.

Many patients show great susceptibility of the skin and fail to react to these measures or feel chilly for some time after them. They should then be stopped at once and a dry rub substituted. Later sponging with warm water, a little cooler each day, may be employed. The morning sponge or bath should never be given with the stomach empty. Vinegar sponges every two hours are useful in some cases.

*Dietetic.*—The diet depends upon the cause of the fever and the state of the digestion. In acute fevers not due to the tuberculous process the diet should be fluid if the fever is high. The chief dependence should be placed upon milk, either plain or diluted. In these acute cases it may be well to restrict the diet for several days, notwithstanding some loss of weight.

In chronic fever, food should be pushed to the limit and solids given freely. Fever rarely abates while the patient is losing weight and the necessity of eating should be impressed upon him. Idiosyncrasies should be given due regard and the patient forced to eat nothing he has an antipathy for, with the exception of meat, eggs, and milk. In high fever and when little food is taken it should be given regularly during the night if the patient is awake. In all cases a glass of milk or an egg should be taken at night if the patient awakes. This is said to prevent the subnormal morning temperature, but does not do so in all cases. Fats and carbohydrates should be supplied plentifully.

*Medicinal.*—The medicinal treatment of fever accomplishes little in most cases. The cause is not affected by drugs and in many instances prolonged use of antipyretics is decidedly injurious. There are, however, some cases in which the heat-regulating mechanism appears to maintain the temperature of the body at a level higher than normal. In such cases the use of antipyretics for two or three days is often followed, in a short time if not immediately, by a fall of the temperature. They should not be used, however, until the fever has persisted for two weeks and are of little avail unless the patient is at rest. In some cases where a rise of temperature just before a meal prevents the patient from eating, or a rise at night prevents sleep,

a judicious use of antipyretics often helps the appetite and prevents the insomnia. The most satisfactory and the least depressing antipyretic is pyramidon. Two grains given in capsules, at 9, 10, and 11 A.M., are often sufficient to bring about the results before mentioned. Five grains may be dissolved in a tumbler of water and sipped throughout the day. In some patients profuse sweating follows the exhibition of the drug in capsules, but is less likely to occur if taken gradually in the watery solution. Pyramidon-camphorate is said to be beneficial in night-sweats.

Besides pyramidon many antipyretics have been suggested. Antipyrine, 3 gr. (0.2 gm.) q. 4 h.; aspirin, 5 gr. (0.34 gm.) t. i. d.; acetanilide, phenacetin, and many others have been recommended.

A tablet compound of acetanilide, gr. 2 (0.13 gm.); camphor monobromate, gr. 0.5 (0.03 gm.), and caffeine citrate, gr. 0.5 (0.03 gm.), often reduces the temperature, and even when failing to do this may prevent the disagreeable chills and sweats which often accompany it. The use of arsenic is said to prevent chills. The antistreptococcic serums have seemed to benefit a few patients, but have not yet passed the experimental stage.

**Chills.**—Hot drinks and avoidance of exposure often prevent a chill.

**Cough.**—This demands careful attention, but probably no symptom receives more rule-of-thumb treatment. The patient should have fully explained to him what will produce the cough, the value and necessity of controlling it, and that every physical means and all simple remedies should be tried before resorting to other measures. Inhalations and intratracheal injections should next receive attention, and lastly sedatives.

*Prophylaxis.*—A patient with persistent cough should be warned against all acts of overexertion, such as rapid and loud talking, laughing, singing, rapid walking, running, and hill climbing. He should avoid all irritants, including very dry air, vapors, smoke, dust, and drinks. Tobacco may have to be forbidden. Sudden changes of temperature, if too great, may excite cough and should be avoided if possible.

There is no more important factor in the treatment of cough than its proper *discipline*, first advocated by Galen. The patient should have fully explained to him that it is not necessary to raise the sputum from the lungs, for cilia are provided for that purpose, and every cough is an act of exertion and may further injure the lungs. The amount of exercise entailed in coughing should be made clear. Cough often begets cough and a tendency once repressed may mean escape from a violent attack.

In every instance the *cause* should be determined when possible. If the cough is due to the pulmonary lesion it must be controlled by appropriate treatment in many patients in order to prevent the discomfort or complications that may arise. Physical methods should first be tried. Deep breathing, ten slow deep inspirations followed by slightly stronger expirations, Cornet found useful. Holding the breath may help. Rest in bed for a patient suffering while up and about with excessive cough is very effectual at times. Change of position has often a marked effect, and a patient who while in bed cannot eat when he sits up, on account of cough, should assume this position for a longer or shorter period, one-half to one hour, before meals. Cough due to pleurisy or fever is relieved by appropriate treatment of these symptoms, *e. g.*, strapping the side or the use of pyramidon at bedtime.

Many simple household remedies are very effective. Sips of cold water,

an occasional bit of ice, sugar-water (irritating to some), a bit of orange or its juice, some form of lozenge, such as glycerin, slippery elm, mentholated, marshmallow, licorice, lactucarium, Iceland moss, malt (bonbons), althea, gum arabic, may each prove useful in some cases. The patient should be impressed that to eat any of these lozenges freely may prove disastrous. Counterirritation has long been employed. A blister or painting with tincture of iodine under the clavicle on the affected side may give some relief, but blisters should never be used if albumin or vesical irritation be present. Suitable dietetic treatment may greatly lessen the cough, and the effect of cod-liver oil in young individuals is well known.

An effectual *morning cough* should never be checked, but may be aided by the use of a cup of hot water with or without a teaspoonful of brandy or 20 drops of the aromatic spirit of ammonia and 5 gr. each of sodium chloride and sodium bicarbonate. Hot milk may be used instead of water.

*Night Cough.*—Many patients who cough on change of position experience some trouble on lying down. Hot water or milk one-half hour before bedtime may lessen this. The bed should always be warm. An incessant cough that prevents sleep must be checked, for a time at least, at almost any cost, and when other measures fail a sedative cough mixture should be used. The cross-binder may afford considerable relief and is worthy of trial.

The attacks of *paroxysmal cough* are often difficult, but most necessary to check. Absolute rest in bed may bring relief, but to control the cough when once it starts, recourse must be had to some inhalation, hypodermic injection, or quickly diffusible anodyne. A few crystals of menthol vaporized in a spoon over a match and inhaled, and the inhalation of a few drops of chloroform and various mixtures, may all be tried. Morphine should not be injected hypodermically; a few drops of laudanum upon the tongue may control the attack. The continual use of the respirator may help.

The *emetic cough*, causing a patient to vomit food he has swallowed with great difficulty and often leading to great emaciation, is serious. Here too rest in bed for a time and in all cases avoidance of exertion after meals, may be beneficial, but limiting the fluids, especially hot drinks, at mealtime, and taking hot water as advised for the morning cough half an hour before meals and coughing up the collected secretions before meals, is often sufficient. In some instances the odor or the taste of the sputum causes nausea or irritates the pharynx. Here, besides deodorizing inhalations, the pharynx may be painted with various solutions (antipyrine, 20 per cent.; cocaine, 5 per cent.; sodium bromide, 20 per cent., etc.). The wheezing so often complained of, especially at night, may be relieved by expectorants or by the use of belladonna, cannabis indica, or stramonium. It is often difficult to relieve.

Intratracheal injections and inhalations are chiefly of use in the treatment of cough and expectoration. Injections of menthol, creosote, guaiacol, iodoform, oils of eucalyptus, thyme, and cinnamon in olive oil, have been used with success in cough uncontrollable by other methods, and seem at times to render the sputum more fluid.

*Inhalations* often markedly benefit the cough, especially when the irritation is in the larger bronchi. The oronasal respirator (Yeo), which can be worn continuously, is probably the best means of administering vapors. A croup kettle, the simplex atomizer, or a tin vessel with a towel for a cone, answers for hot steam inhalations. The following simple formulæ may be tried:

*Sprays.*—Menthol (1 per cent.) and oil of pine (1 per cent.) in albolene or benzoinal, tannin (2 per cent.) in water, or liquor ferri subsulphatis (10 to 20 per cent.) in water.

*Inhalations.*—Croup kettle, etc. Compound tincture of benzoin (1 to 128 of water), carbolic acid (2.5 per cent.) in water, or creosote, eucalyptus, oil of pine, or oil of turpentine.

*Oronasal Respirator.*—Equal parts of creosote and spirits of chloroform; eucalyptol and ol. pini sylvestris, āā ℥iij; spirit of chloroform or alcohol, to ℥j (10 to 20 gtt.); or, fluidextract of conium, 1 to 3 minims in alcohol.

There are certain periods when the administration of *sedatives* seems to be the choice of the lesser of two evils, and many of the milder ones may be used continuously for long periods. Cherry-laurel water, syrup of wild cherry, and hydrocyanic acid, usually in combination with other drugs, are of value. Chloroform, chloral, and the bromides may prove useful. Indian hemp, belladonna, hyoscyamus, gelsemium, aconite, have been advocated and may be carefully tried.

The routine administration of sedatives should be avoided if possible, as the respite from cough obtained by the use of opiates is bought with a price. Morphine should be used only in the terminal stages unless all other sedatives fail to give relief. It should be administered by mouth as a powder, or in fluid until all hope is lost, then hypodermically. Of the opiates, codeine, gr. ¼ (0.016 gm.), heroine, gr. $\frac{1}{12}$ (0.006 gm.), dionin, gr. ¼ (0.016 gm.), are the best. The smallest possible doses should be given, and it is a good plan to change from one to another. Dover's powder (gr. v to xv), a few drops of the deodorized or benzoinated tincture of opium, often help when codeine and its allies fail.

**Expectoration.**—This is closely connected with the treatment of cough, and various procedures to alter the amount or the consistency of the sputum often aid materially or even check the cough entirely. The object of treatment is to aid in expelling the sputum or to lessen its amount. To aid in expelling the sputum many physical methods have been employed.

*Exercise.*—When permissible, walking slowly on the level, up slight gradients, and up stairs, all aid expectoration materially. The exertion of dressing and undressing often facilitates it unnecessarily and undesirably. Simple respiratory exercises, taken between meals, or while walking, such as slow inspiration and expiration, with concomitant movement of the arms up and down, may help in raising the sputum. Passive exercises in the pneumatic cabinet no doubt help some patients.

*Position.*—Change of position often greatly facilitates the expectoration and should be more frequently employed therapeutically. Massage of the chest may aid mechanically and helps the circulation (Moeller). Percussion with a silver paper-knife is attended with good results (Erni), and the value of hydrotherapy, especially the cross-binder at night, is well known.

*Inhalations.*—These often loosen the expectoration and are in some instances almost specific for the fœtor. The steam moistens the air of the room, and when saturated with balsams or carbolic acid renders the sputum less tenacious. Inhalations of creosote under a tent, or of carbolic acid (2.5 per cent.) from a vaporizer or croup kettle, are very efficacious.

*Medicinal.*—The value of hot drinks is marked. The ammonium salts (chloride, gr. v to x [0.3 to 0.65 gm.]; carbonate, gr. ij [0.15 gm.]) or the aromatic spirit of ammonia are probably the best expectorants for general use.

Squills and senega are of value. Ipecac, apomorphine, and pilocarpine are of less value. Citric acid or its sodium salt may be tried when other means fail. Potassium iodide, gr. v (0.3 gm.), and hydriodic acid in syrup are often helpful. Digitalis and camphor, when the heart is weak, are often of considerable value. To lessen the expectoration as well as the cough the so-called false specific, creosote and its derivatives, are excellent. Dilute hydrochloric and sulphuric acids and atropine should be tried in distressing cases.

**Hæmoptysis.**—In severe hæmoptysis from a ruptured aneurism, treatment is often of no avail, for death follows too quickly. The slighter forms tend to cease in spite of almost any form of treatment that is not too heroic, a fact which leads many to put faith in some line of treatment. When conscientiously put to trial no method of treatment, as yet suggested, is helpful in every case.

The chief danger in many patients is aspiration of infected blood into healthy parts of the lung through fear and unnecessary excitement and exertion. The first duty is to calm the fears of the patient and his family. There should be no bustling or hurrying, no whispering, and the physician should assume the ordinary tone of conversation. In an initial hæmoptysis only a cursory examination (inspection and auscultation) of the front of the chest should be made until the patient is up and about.

The patient should assume at once a semirecumbent position, which favors the gravitation of the blood to the limbs and facilitates expectoration. The room should be well ventilated, and cool (45° to 60°) and sufficient, but not too much, covering should be used. Talking should be forbidden, only the necessary attendants allowed in the room, and the cough repressed as much as possible. Small pieces of ice held in the mouth often aid in this, but too much ice may completely upset the stomach. An ice-bag should be placed over the heart. Application of cold to the genitals has been suggested. In severe attacks the patient must be made to lie absolutely quiet, and not allowed even to feed himself.

The diet in slight or moderate hæmoptysis should be non-stimulating and cold or warm (never hot). Fluids should be restricted, and all alcohol, tea, coffee, or chocolate forbidden for some days. Acids are very grateful to many patients and help quench the thirst, but prolong the coagulation time. Six glasses of milk (40 to 50 ounces) and 6 raw eggs for the first twenty-four hours is the best diet. This should be given at frequent intervals and in small quantities, but not begun until several hours after the hæmoptysis. The second or third day it is well to add beef juice, jelly (gelatin), and meat sandwiches (scraped raw meat if possible), and then go back to a solid but restricted diet as soon as possible.

In severe hæmoptysis it is wise to restrict the fluids greatly and to place the patient for several days on a very limited diet.

To limit the volume of blood in the lesser circulation many methods have been employed. In the first place the skin vessels should always be protected against cold, especially sudden cold, *e. g.*, such as changing sheets in a cold room. Ligatures can be applied to three limbs at a time and changed in rotation, one every twenty minutes. The pulse should not be obliterated and the ligatures should be loosened gradually and not left on too long.

To increase the resistance on the proximal side of the point of rupture would necessitate constriction of the pulmonary vessels. The wall of the bleeding vessel, as has been mentioned, is always diseased, and it is futile to

base any treatment upon producing any change in the diameter of the affected vessel. Consequently, we can hope to gain little by drugs producing vasoconstriction (ergot). Adrenalin in slight, oozing hæmoptyses by subcutaneous injection or by mouth is held by some to be of value.

Drugs that reduce the blood pressure in the radial arteries have been of service. The nitrites have long been used. Flick has advocated the use of nitroglycerin in hæmoptysis since 1898, controlling his results by observation of the accentuation of the second pulmonic sound. He uses the alcoholic extract of nitroglycerin in 0.5 to 1 drop doses every one-half hour when necessary. Francis Hare first called attention to the value of amyl nitrite in hæmoptysis, suggesting its supposed vasodilating properties and the reduction of the pulmonic pressure as its method of action. Amyl nitrite, when exhibited in doses sufficient to produce its physiological effects, is of marked benefit in some cases and should always be used at once. If it fail to act advantageously when thus used it should be discarded. Pearls of 3 or 5 drops may, if useful, be put safely into the hands of the patient.

Sodium nitrite lowers the systemic pressure, and if the pressure in the pulmonic system vary directly with that in the radial artery (a point not yet proved) this nitrite would ensure a lowered pulmonary tension for two or three hours. The great difficulty lies in the fact that it is difficult to tell just when to repeat the dose. It is dangerous to lower the blood pressure too much and unwise if beneficial not to lower it enough. Observation of the accentuation of the second pulmonic may be of value in some patients, but to overcome these difficulties more surely the systolic blood pressure should be taken every two hours and the doses ordered accordingly, aiming to keep the tension within certain limits. Practically, it is wise if the patient is very nervous to administer codeine, gr. $\frac{1}{4}$ (0.016 gm.), or morphine, gr. $\frac{1}{8}$ (0.008 gm.), hypodermically, and along with it sodium nitrite, gr. j (0.065 gm.).

Hæmoptysis frequently occurs in the early morning hours and the patient awakens spitting blood. Howell's theory of sleep offers a striking explanation of this phenomenon. This observer holds that sleep is due to the fatigue of the vasoconstrictor centre (or centres), and he has shown by the plethysmograph that a dilatation of the peripheral vessels occurs during sleep. In the early morning hours, when the vasoconstrictor centre is regaining its lost tone, remarkable vacillations occur in the plethysmographic records, which would indicate considerable variation in the quantity of blood supplied to the right side of the heart, and concomitant variations in the pulmonary blood pressure Sudden variations in pressure are probably more dangerous than a steady high pressure. To prevent these variations as much as possible and to equalize the blood pressure, it is well to give morphine and sodium nitrite hypodermically between midnight and 2 A.M., waking the patient if necessary.

Aconite has been suggested in hæmoptysis, and its use, when controlled in the foregoing manner, may prove to be very beneficial. It also reduces the force of the heart and slows it.

In long-continued hæmoptysis, chief reliance will, however, have to be placed upon restriction of the diet, with occasional doses of the nitrite. This would seem to be the most rational medicinal method of regulating the blood pressure, but it does not control all hæmoptyses. The administration of nauseants (apomorphine, tartar emetic, ipecac, antimony, etc.) for this purpose is hardly to be recommended although the use of table salt, either

a teaspoonful, or in a supersaturated solution with ice, is a favorite remedy of many patients.

Atropine in doses of gr. $\frac{1}{120}$ (0.0005 gm.) may be given hypodermically every four hours for a time in severe hæmoptysis, or, if well borne previously, gr. $\frac{1}{60}$ (0.001 gm.). Weismayr, who believes it reduces the blood pressure, has given it in doses of gr. $\frac{1}{250}$ (0.0025 gm.). Digitalis raises the blood pressure, but slows the heart and steadies it, and in some cases of prolonged or slight hæmoptysis, due probably to congestion, seems to be of especial value.

The coagulation time of the blood in hæmoptoic cases has not been determined as far as can be learned. Calcium salts have been suggested to increase the coagulability. In many hands they have not given any striking results. The lactate in doses of gr. xv to xx (1.0 to 1.3 gm.) should be given in water three times a day or gr. xxx (2 gm.) administered night and morning for three days. Lime-water, added to the milk, has also been employed for the same purpose. If the coagulation time of the blood cannot be followed the calcium should be given three days and omitted two (Boggs). Acids, such as lemonade, should be avoided, for they prolong the clotting time of the blood. The subcutaneous injection of gelatin is not recommended. It may be given by mouth.

Turpentine has been warmly recommended and is said to increase the coagulability of the blood as well as to possess astringent and vascular depressant (?) qualities. Dilute sulphuric acid is said to aid coagulation.

*Limiting the movement* of the chest has been advocated. No doubt the ice-bag may owe some of its value to the limitation of movement it causes. Strapping the affected side has been suggested, but it is by no means easy in all cases to detect the origin of the blood. Cayley, in 1853, suggested putting the affected lung at rest by producing a pneumothorax, and Murphy has advocated the injection of sterile nitrogen gas. Besides the use of the ice-bag, and possibly of sand-bags, little real advantage is to be gained by limiting the pulmonary movement unless excessive, and if it prevents the expulsion of the blood, harm may arise.

While the value of rest cannot be overexaggerated in the treatment, *exercise* is not always highly injurious. Several observers have recently adopted, and with excellent results when prolonged rest was of no avail, carefully graded exercises for patients with slight, but persistent, hæmoptysis.

If the sputum be merely blood-tinged, or slightly streaked, and if hæmoptysis has never occurred before, the patient, if in an incipient stage, should be cautioned against any exertion for a few days. Such an occurrence, however, in an advanced stage demands rest in bed.

*Narcotics.*—Morphine, and less effectually codeine, help to produce absolute rest, quiet the circulation, check the cough, and so help in the formation and protection of the thrombus, but their use is not unattended with danger. This very quieting effect may result in producing areas of bronchopneumonia due to retained blood and secretions. For patients laboring under excitement, with a bounding pulse that cannot be quieted by other means; for those with great fluctuations in the blood pressure, and particularly in those cases where hæmoptysis seems to recur during the night or early morning hours, morphine is invaluable. To attempt to reduce the respirations to a low number (10 to 12) cannot be recommended. When used it should be given hypodermically in doses of gr. $\frac{1}{8}$ (0.008 gm.) and in a few instances for one or two doses of gr. $\frac{1}{4}$ (0.016 gm.). It may occasion-

ally be necessary to give it every four hours, but as a routine, codeine, gr. ¼ (0.016 gm.), should always be preferred unless it excites the patient.

The use of astringents cannot be upheld. The question of stimulation after hæmoptysis frequently arises. Digitalis, strychnine, camphor (oxyphor), and alcohol have been used. The latter should be sparingly given. A low blood pressure, it must not be overlooked, is conducive to thrombosis.

The lost blood is quickly regained in patients with a favorable prognosis, and it is rare that any treatment for anæmia is required. There is some prejudice against iron, which should, however, be freely used if necessary.

*Complications.*—The treatment of many complications must be modified, and it is unwise to aspirate a pleuritic effusion if the sputum be blood-tinged. In one patient suffering from hæmoptysis appendectomy was successfully performed.

*Surgical Treatment.*—The excision of one or more ribs over a cavity, when persistent hæmoptysis is present, has given little permanent relief.

*Prophylaxis.*—This is of considerable importance, and every patient who has had hæmoptysis should be warned of its recurrence. Patients who have had repeated hæmoptyses should exercise with great caution, and all violent respiratory movements must be forbidden. Women who have premenstrual hæmoptysis should remain in bed during this period.

If the occurrence of the pneumococcus be as frequent in the blood as some affirm, it would be advisable that in sanatoriums all new patients be isolated as much as possible for a few weeks and longer if pneumococci are abundant in their sputum. For the same reason all patients with hæmoptysis should be isolated.

**Night-sweats.**—The hygienic-dietetic treatment greatly decreases their frequency. The hygiene of the skin should receive especial attention. The patient should wear woollen night-robes and in cool weather sleep between blankets, but should carefully avoid too much covering, especially over the feet. When possible the patient should be given an alcohol or dry (with flannel) rub after being thoroughly dried.

When sweats occur in weak patients, nourishment should be frequently administered, especially at night whenever the patient is awake, and in some instances he should be aroused and food given two hours before the expected sweat. Two or three drachms of brandy in the milk given at bedtime is often better than plain milk. Sponging at bedtime with an ounce of toilet or table vinegar, or of eau de cologne, in a pint of water, or even with pure vinegar, is very effective in many cases. Combined with equal parts of alcohol (95 per cent.), the commercial formalin (40 per cent.) has been painted on the skin every day. Its application should never be entrusted to the patient. Various combinations of formalin in powders have given some relief when dusted on the skin. Salicylic acid has been employed successfully as a powder (salicylic acid, 3 parts; starch, 10 parts; talcum, 87 parts).

A cold compress to the entire chest worn all night, or an ice-bag applied to the abdomen for several hours in the evening, lessens the sweats in many patients who get relief in no other way.

Medicinal treatment should be resorted to only when all other measures have failed. Camphoric acid, gr. xij (0.8 gm.) at bedtime, should be first tried and the cough treated if necessary. Zinc oxide, gr. iij to v (0.2 to 0.35 gm.) at bedtime; aromatic sulphuric acid, ℥ss (2.5 cc.) at bedtime, may both be tried; but in many cases it is wise to use atropine, either alone or in

combination with a little morphine and a mineral acid, atropine, gr. $\frac{1}{120}$ (0.0005 gm.); morphine, gr. $\frac{1}{6}$ (0.004 gm.); aromatic sulphuric acid, ♏ xv (1 cc.); syrup tolu, to ℥j (5 gm.), at bedtime. Much larger doses of atropine, gr. $\frac{1}{100}$ to gr. $\frac{1}{12}$ (0.0006 to 0.005 gm.), may be required.

**Dyspnœa.**—The treatment of dyspnœa is very unsatisfactory in many cases, and every effort should be exerted to determine its cause. Complications should receive appropriate treatment, which is often markedly beneficial.

When, however, these conditions are excluded there remain many distressing cases of dyspnœa, such as those caused by rapid extension of the disease and by mechanical factors. In patients with arrest and a thickened, adherent pleura much can be accomplished by properly regulated breathing exercises, or walking up slight ascents. The latter helps many patients without apparent pleuritic adhesions. Patients with advancing fibrosis and small pulmonary capacity should be told of their limitations, which they should not exceed. If due to weakness or to great difficulty in raising the sputum, stimulants and expectorants may be used. Oxyphor (an alcoholic solution of oxycamphor), in doses of 10 drops on a little sugar every three or four hours, often affords the greatest relief. There are, however, patients to whom these measures afford no relief, for whom heroine soon loses its effect, but who are markedly relieved by the use of morphine in very small quantities. It should be reserved for patients in the very last stages or for those acutely ill. The indications for the use of oxygen and of morphine are very similar.

**Tachycardia.**—Rest in bed or on a reclining chair has a marked effect, and should be insisted upon in all early cases when the pulse is persistently above 100. Severe exercise, excitement, coffee, tobacco, alcohol, and all indigestible food should be avoided. Carbohydrates and in some cases all food may have to be limited. If cardiac distress or palpitation occurs, an ice-bag over the heart is often sufficient. Bromides, valerian, chloroform, and menthol may be of service, but digitalis and caffeine are of little value. Creosote and opium are said to increase the tachycardia and heroine to quiet it. Local application of electricity to the neck is helpful in some cases. Low, warm, moist climates have been recommended. Abrams has found the Schott treatment to produce a phenomenal improvement in tuberculous patients who resisted other methods of treatment.

**Pain.**—*Pleuritic.*—The treatment consists chiefly of immobilizing the side and in counterirritation. Acute pleurisy demands rest in bed and the cough, when severe, should be checked. A few patients with arrested disease obtain relief by carefully regulated hill climbing, which with proper breathing exercises often partially overcomes the resulting deformity.

In acute attacks the side should be strapped with zinc oxide adhesive plaster. The straps (two or three in number) may be applied about the thorax during full expiration, reaching two or three inches beyond the midlines, front and back, or one or two straps, if the pleurisy is in the axilla, may extend entirely around the thorax. Much greater compression can be obtained in this way. A canvas jacket made with stays and laces with straps reaching over the shoulders affords great relief to some patients. Corsets help some women.

*External Applications.*—Heat or cold may be applied, the latter best in the form of an ice-bag. Cold compresses may be tried when this is not at hand. Cold sponging in the morning need not necessarily be abandoned. Wet cups and leeches are now little used and dry cups have little effect upon some

patients. Liniments are often useful and mustard poultices, mustard leaves or papers, or painting with the tincture of iodine, are all of value. It is wise to apply the mustard or the iodine to a number of small areas of skin about the size of a postage stamp, leaving fully as large an area between for future applications if necessary. Ointments containing menthol, belladonna, and opium may be rubbed in. The cautery, lightly applied, is far superior to most applications. A blister under the clavicle may aid when the pleurisy is in this region. Cloths kept moist in a saturated solution of magnesium sulphate and applied for some hours over the painful area may be very helpful (Tucker).

*Medicinal.*—Sodium salicylate up to ʒiss (6 gm.) per diem if necessary, followed by smaller doses, gr. viiss (0.5 gm.) with or without potassium iodide, is held by some to be almost specific. Aspirin, acetanilide, and phenacetin are helpful, and, finally, in a very few cases, morphine must be used.

**Hyperæsthesia.**—The treatment of this is very unsatisfactory. Massage, local hydrotherapy, electricity; belladonna and opium plasters; iodine locally; ointments of veratrine, of chloral, cocaine, and menthol; and chloroform in oil may be used. Often the condition requires no treatment save a word of encouragement.

**Treatment of Complications.**—This interferes little in many cases with the general treatment. As a rule it is easy to decide whether or not, for the time being, the outdoor life must be abandoned; if any doubt arises it is wise to treat, first, the pulmonary lesion. The patient if confined to bed should be placed in a room which opens on a porch upon which the bed may be moved.

**Ear.**—As soon as the drum perforates in tuberculosis of the middle ear the external canal should be washed with warm boric-acid solution or a 1 to 5000 bichloride solution and the canal dried. When the discharge becomes scanty, boric-acid powder may be insufflated. The canal may be packed with iodoform gauze twice daily (by the patient).

**Nose.**—Obstructions should be removed as soon as the patient's condition warrants it. Tuberculous ulcers should be treated by scraping, followed by lactic or chromic acid.

**Influenza, Coryza, Bronchitis.**—The patient with influenza should be isolated and repeated attacks would suggest the advisability of the isolation of the organism and vaccination if such treatment prove successful. If fever be present, the patient should be in bed. In catarrhal conditions of the upper air passages the patient should remain indoors until the acute stage is over. For the intercurrent attacks of coryza, leading often to laryngitis, tracheitis, and bronchitis, a full hot bath (110° to 115°) at night, followed by a cold spray, the use of salol, of a mixture of liquor ammonii acetatis, ʒij (8 cc.); laudanum, gtt. x (0.6 cc.); sweet spirit of nitre, ♏xv (1 cc.); and camphor-water, q. s. ad ʒj (30 cc.), every four hours, may abort the attack. The tightness and soreness in the chest are best treated by a mixture of the wines of ipecac and antimony, āā gtt. ij to v; sweet spirit of nitre, gtt. x to xx; and liquor ammonii acetatis, q. s. ad ʒj (4 cc.), every three or four hours, until these symptoms are relieved. For the succeeding bronchitis after the acute stage is passed, nothing is better than creosotal (♏v) after meals. The cold chest bath should be practised each morning throughout the attack. A drop of the tincture of aconite every hour for a few doses often aborts a cold. During these attacks the patient should be isolated.

**Pleuritic Effusion.**—Delafield has recently advocated paracentesis as soon as effusion is diagnosed. Sweating, purging, and restriction of fluids may be tried in chronic cases. Careful respiratory exercises should be begun as soon as the fever abates.

**Empyema.**—Petit advocated incision when the empyema contains other organisms, but when tubercle bacilli alone are found he has had good results by aspiration and the injection of 1000 cc. of a solution of 0.5 per cent. iodine and 0.5 per cent., of potassium iodide, some of which is left within the pleura. West has recently combated the widespread idea that incision hastens the fatal termination, and advocates free incision and drainage as soon as the diagnosis is established. Operation does at times hasten the end, and, when decided upon, should be done under local anæsthesia, and, if necessary, resection of a rib be practised later. When incision is employed, methods to expand the lung should be used as soon as the pain permits.

**Pneumothorax.**—This admits of little choice at first; later the treatment may be conservative or radical. Absolute rest in the reclining position, application of straps or hot flannels, morphine (to be administered with great caution) for the pain; the diffusible stimulants, ether and brandy, aromatic spirit of ammonia, digitalis or strophanthus if collapse set in, and amyl nitrite, should be tried when the symptoms are urgent. It may be necessary to relieve the tension of the air at once, and, if the opening be valvular, West's method of leaving a needle *in situ*, from which a rubber tube runs into a vessel of sterile water, may be employed advantageously. Mild purgation should be used after the first day. Absolute rest is most important. When effusion takes place quickly it seems undoubtedly wise to refrain from aspiration for several days, and then it should be removed with as little suction as possible. The siphonage method should be tried. The use of two needles and washing out the pleura with boric-acid solution Fowler finds helpful in many cases. Thoracotomy and even thoracoplasty may have to be resorted to, especially when pyopneumothorax supervenes. As this almost always results fatally, and as many hold radical operative interference hastens the end, it should be carefully considered. West strongly advocates incision in such cases and reports good results.

**Secondary Infections.**—Removal of the patient to localities where such infection is less likely to occur is the most rational, and the separation of patients with from those without fever has been suggested (Sata). The many health resorts, the open sea, sparsely inhabited localities in many parts of the country (even the suburbs of large cities) are to be preferred to the congested areas.

Antistreptococcic serums have been strongly advocated and special forms have been prepared by Menzer, Aronson, and many others. The results up to this time have not been very satisfactory and the treatment is not entirely devoid of danger. A vaccine, made from organisms from washed sputum, to which the patient's opsonic index is low, has been found of value, especially in chronic stages with abundant sputum.

Creosote and its derivatives are very effective in some cases. Flick uses pure beechwood creosote in large doses (gtt. xx to xxx, t. i. d.), and gives it one-half hour before meals in hot water, a tablespoonful for each drop, an amount which is reduced when 10 to 15 drops are reached.

Inhalation of vapor from carbolic acid (2½ per cent. in water) for fifteen minutes night and morning, as well as of creosote, have all been recommended

and may be tried. The use of tuberculin, of lutol, of antituberculous serums are said to be contra-indicated in secondary infections. In many cases we can do nothing but maintain the general health.

**Chilblains.**—Hot-water bottles and soapstones should be avoided. Application of tincture of iodine in flexible collodion (3j to 3j) every night for some days, or of ichthyol ointment (10 per cent.), may be tried. Calcium lactate (gr. lx daily) sometimes prevents these serous hemorrhages.

**Anæmia.**—In the majority of cases the hygienic-dietetic treatment is all that is required. In many patients the pallor is due to the small volume of the blood, not to lack of hæmoglobin. Nothing, however, is more efficacious than Blaud's mass with gr. $\frac{1}{6}$ (0.012 gm.) of the extract of nux vomica after meals. Fowler's solution, gtt. ij or iij, p. c., and arsenate of iron, gr. $\frac{1}{8}$ (0.008 gm.), are also helpful. A decided change of climate, especially to high altitudes, when the anæmia is not very severe, has a marked benefit.

**Gastro-intestinal.**—The local treatment of tuberculous processes in the oral cavity has not been satisfactory. Complete and in some cases even partial excision has cured tuberculous disease of the tongue, but such radical steps can rarely be advocated in advanced stages of pulmonary tuberculosis. All causes of irritation should be removed or avoided, *e. g.*, carious teeth, smoking, irritating or hot food, and even talking in some instances. Lactic acid (30 to 50 per cent. at first) may be tried. Morphine and cocaine may have to be used freely.

**Digestive Disturbance.**—Every means should be used to determine the cause, which in not a few instances is overfeeding. Lavage need not be feared except in case of a recent hæmoptysis, and a test meal should always be given in prolonged disturbances. Examination of the fæces may reveal the cause of the intestinal disorder.

*Prophylaxis.*—Many patients have to be taught how to expectorate. This is especially true of women, who for months swallow their sputum unconsciously. This sputum may cause a simple diarrhœa, almost impossible to control, or tuberculous enteritis as well as re-infection of the lung.

*Flatulence.*—The treatment of this symptom should be at first dietetic. All fluids at meals should be avoided unless at the very end. Milk may have to be modified or even given up for a time and the diet restricted largely or wholly to albuminous food. Often omitting milk and a course of calomel suffices. Effervescing waters should be avoided.

*Dilatation of the Stomach.*—This very troublesome complication is difficult to meet. The fluids should be limited as much as possible, the abdomen may be supported with straps, the patient should lie on the right side at intervals for one or two hours after meals, and finally recourse may be had to daily or semiweekly lavage.

*Vomiting and Nausea.*—It is wise for a few days to put the patient in bed, restrict the diet to peptonized milk, hot or iced, or feed per rectum. This together with lavage is often sufficient. If symptoms of dyspepsia have been noted, the diet may have been too bulky, or fermentation and decomposition may have occurred, with subsequent irritation. Gastric sedatives are indicated. For nausea, restriction of food, drop doses of the tincture of nux vomica every fifteen minutes, and other remedies used for vomiting may be given. As it is impossible to differentiate between a simple and tuberculous ulceration, the treatment for simple ulcer should always be followed, but in the open air, if possible.

*Anorexia.*—Rest out-of-doors is sufficient to restore a lost appetite in many patients who have been at work. If too prolonged rest has been followed, carefully regulated exercise is often helpful. All lunches between meals should be stopped and if the anorexia is pronounced the patient should be put to bed and fed on liquids. Feeding per rectum may be resorted to for a time and Debove's method of suralimentation may be used, but the second state of such patients is often worse than the first. The most important factor is often a complete change of surroundings and of table. If fever be the cause, antipyretics may be used advantageously, especially pyramidon. Bitter tonics, as nux vomica or the alkaline gentian mixture, may be given. A little Vichy before meals or a little whisky or wine with the meal often aid. A drop or two of creosote in water before meals may stimulate a flagging appetite. The false appetite, a desire for food until the first few mouthfuls are taken, when all appetite is lost and nausea may appear, may be benefited by nux vomica or dilute hydrocyanic acid before meals. Dysphagia from pharyngeal or laryngeal ulceration, anorexia from excessive cough, or other complications must receive appropriate treatment.

*Constipation.*—Every other means should be tried before drugs. The quantity of water, especially between meals, must be sufficient, and the patient should eat freely of fresh and preserved fruit. Massage of the abdomen relieves some. Glycerin suppositories and enemata of olive oil at bedtime may be effective. The large amount of food consumed makes the condition of the bowels of great importance, and an occasional dose of castor oil, of calomel and a saline, are in some cases a necessity and aid most patients. The fluidextract of cascara, when good, is the best medicinal treatment. Large doses should be given at first and always in a considerable quantity of water. Effervescing sodium phosphate is also of value. In a few patients many drugs have to be used.

**Intestinal Tuberculosis.**—The treatment of this is usually unsatisfactory. In all severe cases the patient should be kept at rest and in bed for a time at least. The diet is of the greatest importance and every detail should be attended to. All fruits, fruit juices, salads, most vegetables, sugar and other sweets should be avoided. Beef juice, egg-yolks, and certain prepared foods may increase the diarrhœa. If severe, the diet should be much restricted and limited to boiled milk and albumen- or rice-water for a few days. Fluids should be restricted and cold drinks avoided. Tea, cocoa, and bean coffee may be taken in moderate quantities. Lime-water or cognac may be added to the milk or it may be peptonized or given as koumyss.

Saline irrigations are useful and a few drops of laudanum may be added. Mueller warmly advocates an injection of ʒj to ij (4 to 8 gm.) of bismuth subnitrate in 250 to 300 cc. of warm water, to be retained for ten to fifteen minutes, preceded by a cleansing enema. A few drops of laudanum may be added when necessary. An abdominal band of flannel or silk should be worn night and day. Local applications to the abdomen may give great relief, and turpentine stupes, repeatedly applied, often relieve the severe abdominal pain. An ice or hot-water bag may in some instances be helpful. A limited resection, especially ileocæcal, or lateral anastomosis may afford much and in a few cases permanent relief if the patient can stand the operation. The usual drugs may be employed. Sooner or later the majority have to resort to the use of opium by enema (starch and laudanum) or suppository (opium or morphine).

**Appendicitis.**—The treatment of appendicitis in the tuberculous, whether simple or tuberculous, should be carefully considered. Only an expert anæsthetist should administer the anæsthetic, for in the struggling, vomiting, and subsequent aspiration of secretions into other parts of the lungs lies the chief danger.

**Peri-anal Abscess and Fistula-in-ano.**—Warm, moist applications should be applied until pus forms, when, under a local anæsthetic, the abscess should be incised. In a few instances the abscess heals, but usually a fistula results, which, when the patient's condition warrants a general anæsthetic, and when well defined by scar tissue, may be excised. Fistulæ can exist for years and exert little or no discernible influence upon the general health if carefully and frequently cleansed. The injection of mercurial ointment has in some cases resulted in healing.

**Arthritis.**—Patients with pulmonary tuberculosis and arthritis do better in warm, equable climates. The salicylates, aspirin and salol, are usually well borne, but the joint should first be treated with flannels saturated with oil of wintergreen (synthetic) and covered with oiled paper or silk. Tuberculous arthritis in no way changes the treatment.

**Syphilis.**—This need in no way interfere with the routine treatment. Potassium iodide and mercury are well borne.

**Diabetes.**—A combination of pulmonary tuberculosis and diabetes is, in practically all cases, fatal. The treatment should be systematic and directed against the symptoms causing the patient the most concern, either mental or physical.

**Menstrual Disturbances.**—Amenorrhœa is frequent, and, unless accompanied by some discomfort, requires no treatment. Many patients suffer considerably at this time, and rest in bed should be advised.

**Pregnancy.**—Peter's words may be well applied here: "Fille, pas de mariage: femme, pas de grossesse; mère, pas d'allaitement." Conception should be avoided in all cases where the patient has not been well for at least two years. The dangers of repeated pregnancies should be carefully explained. The financial condition of the pregnant woman is of great importance, and if she must work she must avoid pregnancy. In such conditions artificial sterility has been advocated, but is of doubtful advisability.

When pregnancy occurs, abortion should be considered if the pregnancy is in the first three or four months. In fibroid phthisis, as the disease is not influenced by pregnancy, abortion need not be considered (Edgar). Tuberculous laryngitis and nausea and vomiting in the early stages are always positive indications for abortion, which should be performed by the quickest and least laborious method. At term labor should be allowed to proceed to the beginning of the second stage, when chloroform should be administered and forceps applied. It is difficult to estimate even approximately the mental and physical strain that many patients undergo during labor. This is unquestionably the cause of the rapid spread of the disease following childbirth, and for these reasons the steps indicated should be followed. The mother should not nurse the infant, but a wet nurse may be employed or modified milk be used. It is often well to institute a short course of treatment after delivery in patients whose disease has been long cured.

**Insomnia.**—This may often be overcome by a regulation of the diet and of the bowels. The supper should be light and early. All mental and

physical excitement should be avoided, especially during the evening. The patient should not sleep during the day. The room should be dark, well ventilated, not too cool (40° to 50°), and the bed warm. Some patients sleep much better out-of-doors. A wet pack to the abdomen, legs, calves, or feet, or even a full chest pack may be efficacious. Massage of the back is often helpful. Fever may cause insomnia and the temperature should always be taken at night for a time when insomnia occurs. Appropriate treatment of this symptom or of cough may give good nights. A glass of hot milk, of buttermilk, of beer, or a teaspoonful of whisky (not unattended with danger) often enables a patient to sleep. Veronal, gr. viiss (gm. 0.5), and other hypnotics for one or two nights may aid.

**Medicinal Treatment.**—The natural tendency in slight and early lesions is toward recovery, and even in patients with advancing disease periods of marked cessation of symptoms and improvement of the general condition are not infrequent. From this it is seen how difficult, if not impossible, it is to draw any conclusions from a few patients, especially as "controls" are seldom selected at the onset of treatment. The most potent factor of many lines of treatment lies unquestionably in the enthusiasm of the physician about the remedy he is administering, or, in other words, in suggestion to the patient, most often unintentional.

The "antiseptic treatment," based on the idea that it is possible to destroy the tubercle bacillus *in situ* without harming the tissues, needs only to be mentioned to be dismissed. The view that healthy contiguous parts may be protected in this way has never been proved by clinical experience, either in pulmonary or localized surgical forms of tuberculosis. No medicinal substance has been found to neutralize the tuberculous toxin.

**Creosote and its Derivatives.**—These still stand preëminent among that class of drugs long looked upon as "specific" in pulmonary tuberculosis. They have no action whatever upon the tuberculous process, but in some cases seem to act almost as a specific upon the accompanying bronchorrhœa and intercurrent attacks of simple bronchitis. No scientific study of their effect upon the secondary organisms in the sputum has been made, but their action is no doubt due in part to this and in part to a stimulating effect upon the bronchial mucous membrane during their excretion through it. For this effect small doses only are necessary in most patients, and Sommerbrodt's dictum that the larger the daily dose the better the results cannot be upheld. Drop doses of creosote act in some patients as an excellent tonic for a poorly secreting stomach, an explanation of the benefit of combining it in these quantities with cod-liver oil. Guaiacol, more toxic than creosote, has been used externally for reduction of fever, but in large daily doses it may produce collapse and cannot be recommended. Several instances of poisoning by creosote from the usual doses have been recorded. Among the contra-indications are fever, persistent tachycardia, hæmoptysis, but a persistent taste of creosote, gastric irritation, and nephritis are of real importance. The patient should always be warned to stop it or any medicine if the slightest digestive disturbances occur. Only pure beechwood creosote should be used.

**Arsenic.**—In various forms this has long been used in chronic nervous and wasting diseases. It has been thought by some to exert a specific action in pulmonary tuberculosis and in some it stimulates nutrition remarkably.

**Alcohol.**—The benefit derived from alcohol rests upon its value as a food and upon its effect upon the symptoms or upon the disease itself. The direct effect of alcohol upon tuberculosis is probably not great, but in susceptible and even in robust individuals prolonged overuse of alcohol may weaken the resistance of the body to the tubercle bacillus. The advocates of alcohol have, however, always based their claim for it upon its symptomatic effect.

The objections to its use are numerous and more patients with pulmonary tuberculosis have been harmed than helped by alcohol, especially in cold climates and high elevations. It should never be given for some time after hæmoptysis, nor to nervous, excitable patients. In individuals long accustomed to its use it should be withdrawn gradually until a small amount is taken. If this is not possible it should be proscribed. If it increase cough, or irritate the larynx or stomach, it should be strictly avoided.

In brief, alcohol may he said to be a dangerous food and a symptomatic drug of considerable potential danger, but of value in some cases of pulmonary tuberculosis. In a few patients a cocktail or a tablespoonful of whisky taken with the first part of the meal may aid a flagging appetite or weak digestion. One glass of stout, of bitter ale, or of a good wine may do the same. It should be remembered that, like a tonic, it is not needed when the appetite is good. A small amount of brandy or whisky in milk or sherry with egg is permissible if it enable patients to take these foods who otherwise could not. One glass of beer or ale at bedtime or a little whisky may relieve insomnia, but these are dangerous remedies. Late in the disease brandy and champagne are of great value in some cases, and a few patients with slowly progressing, chronic disease unquestionably prolong their existence by a judicious, although rather free, use of spirits.

A number of substances which increase the leukocytes have been employed. Foremost among these stands cinnamic acid. The same effect has been noted in regard to tuberculin, but nucleic acid stands as the best example of this class. More recently, Ullman and Huggard and Morland have advocated the use of yeast, rich in nuclein, as of value in pulmonary tuberculosis, where it increases the leukocytes and opsonic index, when administered by mouth in doses of gr. l to cl (3 to 10 gm.) of dried yeast in milk twice a day. Brewers' yeast may be used.

**Cinnamic Acid.**—This and its sodium salt (hetol) have been little used outside of Germany. Hetol, when properly administered, produces leukocytosis and an increase of connective tissue about the tuberculous focus. It is said to prevent or replace caseous matter by vascular connective tissue, forming true cicatrices, to increase the lymph flow, the alexins, and thus to produce healing of tuberculous lesions. It has been administered by ingestion, by inhalation, by subcutaneous injection, but preferably by intravenous or intramuscular (intragluteal) injection.

Various salts of calcium (carbonate, bicarbonate, phosphate, iodide) have been given by mouth or hypodermically, alone or in combination with creosote, tuberculin, etc. The calcium salts are said to be deposited at the foci of the inflammation and afford a mechanical stimulus which starts and aids the process of repair (Michelozzi). On account of the demineralization in pulmonary tuberculosis lime-salts are of value, but exert no specific action.

Strychnine, gr. $\frac{1}{30}$ (0.002 gm.), is of value. It acts advantageously upon lowered blood tension, weakened heart, jaded appetite, and neurasthenia.

**Specific Treatment.**—Scientific endeavors to find a specific for pulmonary tuberculosis may be said to have begun in 1882, with the discovery of the tubercle bacillus. In 1890 came Koch's announcement that he had found in tuberculin a specific for the early stages of pulmonary tuberculosis. That full recovery from a localized focus in the glands or skin seemed to confer immunity against pulmonary tuberculosis had previously been noted by Marfan. These facts suggested to Koch the idea of a specific substance in the tubercle bacillus, which in turn led to the discovery of tuberculin.

**Choice of Tuberculin.**—Many observers believe that the majority of tuberculins used clinically are of equal value. The qualifications of the physician who administers it are certainly of more importance in most cases than the quality of the tuberculin (Sahli). The work of Wright and others has shown that heat above 60° C. and chemical manipulation may injure bacterial vaccines. For this reason it would seem wisest to select those tuberculins which have been subjected to the least manipulation.

From theoretical considerations it would seem that the most rational tuberculins named in the order of the dates of their discovery are B. F., T. R.,[1] B. E., and a mixture of B. F. and B. E. B. F. contains the products of the tubercle bacilli disintegrating during the growth of the culture, as well as the unchanged products of the tubercle bacillus given off in its growth, and, while less toxic than O. T. and possibly to be preferred for this reason for febrile patients, it may possess some immunizing properties destroyed by the prolonged heating to which O. T. is subjected. B. E. possesses all the immunizing substances in the tubercle bacillus and is subjected to heat of only 60° C. An emulsion of B. E. in B. F. would, therefore, seem to combine whatever immunizing properties exist in either the tubercle bacillus or the culture fluid. K. Spengler strongly advocates B. F. of bovine origin (his P. T. O.), believing it causes few reactions and better immunity in infections with the human strain of tubercle bacillus. B. E. in large doses may cause sterile abscesses. B. E. and T. R. cause more local reaction at the site of inoculation, but apparently little more frequent, though less readily controlled, general reactions than O. T. or B. F.

Many other tuberculins have been used and possibly are of equal value, viz., O. T., watery extract, Beraneck's tuberculin, and tuberculol. Apparently of less value may be mentioned Trudeau's and Hunter's modification B., tuberculocidin, antiphthisine, purified tuberculin, oxytuberculin, tuberculoplasmin, and tuberculin from fowl and fish tubercle bacilli. Inasmuch as von Behring has not clearly described the preparation of his T. C. and tulaselactin, it is impossible to discuss them.

Tuberculin should be administered to patients who are afebrile and in a state of good nutrition. Many patients who have long followed the hygienic-dietetic treatment seem to reach a state where no further improvement occurs. They no longer have fever, the bodily weight is above normal, but cough, expectoration, and physical signs persist, and tubercle bacilli are still to be found in the sputum. These patients should always be subjected to tuberculin treatment in hope that chronicity may be avoided. It is also indicated in early closed pulmonary tuberculosis, and many have recommended its

[1] Living bacilli were found in these preparations for a short time after they were first put upon the market. The following abbreviations for the various tuberculins are used throughout this article: O. T., Koch's original tuberculin; T. R., tuberculin residuum; B. E., bacillen emulsion; B. F., Denys' bouillon filtré.

use in members of 'phthisical families," who as yet present no evidence of the disease. Children do well under its use.

Patients with persistent slight pyrexia, which rest does not affect, may lose it under tuberculin. If, however, the temperature reaches 101° it is wise to begin with doses smaller than usual, to increase with the greatest caution, and to abandon the treatment if any stubborn intolerance is manifested. In such patients too much must not be expected from tuberculin. It is rarely wise to administer tuberculin to patients whose minimum temperature does not fall below 99° every day. In patients who have had frequent or repeated hæmoptysis great care should be used. In pulmonary tuberculosis with secondary infections, the tuberculin treatment and vaccination against secondary organisms may go hand in hand.

As contra-indications to tuberculin treatment may be mentioned: rapid loss of flesh, malnutrition (so frequent in late stages), meningitis, acute miliary tuberculosis, nephritis (non-tuberculous), epilepsy, pronounced nervousness, and a persistent pulse rate above 100. Excellent results have been obtained in ambulant patients in incipient stages at dispensaries.

The advice to be given patients inquiring in regard to tuberculin treatment is of great importance. It should be frankly explained to them that tuberculin carefully given can produce no harm, but that it may be to them of little or no immediately apparent value.

When tuberculin is administered to many patients, great care should be exercised to avoid spraying the tuberculin in the air when ridding the syringe of small bubbles of air, otherwise severe reactions may occur. The pipettes and glasses used for making dilutions should never be replaced in the boiling water used to rinse out the syringe after each injection, nor should the rinsing water be ejected into this pan. If the physician who gives tuberculin be tuberculous, he should wash his hands as soon as he has finished handling the tuberculin.

The intravenous method, requiring $\frac{1}{10}$ of the subcutaneous dose, has been advised by Koch in place of large doses of B. E., which subcutaneously cause abscesses. Denys has occasionally employed it for B. F. when proper results could not be obtained by the subcutaneous method. In view of the fact that the tuberculous toxin from the focus of disease circulates more freely in the bloodvessels, it would seem more advisable to attempt immunization by subcutaneous injection (lymphatic circulation). The administration of tuberculin for treatment by ingestion, inhalation, or intratracheal injection is not to be recommended. Inunction, as Spengler suggests, or suppository, may be used for a time in patients with great hypersensibility. Klebs and Maragliano, however, both recommend ingestion.

*Dosage and Interval.*—In the proper selection of the dose and of the interval between doses lies the key to the successful treatment. Tuberculin should be looked upon as a most powerful poison, capable of producing irreparable harm in ignorant or careless hands. The slightest departure from the ordinary course of events should be thoughtfully considered. The tolerance to the tuberculous toxin varies greatly (from 1 to 10,000, Sahli) and apparently is independent of sex, of amount of pulmonary involvement, and of general physique.

The beginning dose should always be far below that expected to excite reaction. In febrile patients and in those who have been subjected to the tuberculin test it should be smaller than in others. In 1890 and 1891 the

beginning doses of O. T., *e. g.*, 0.001 cc., advised by Koch, were much too large. Guttmann and Ehrlich, in 1891, and later Petruschky, Trudeau, and Goetsch advised smaller doses (0.0001 or, better, 0.00001 cc. O. T.), which are now accepted as a safe beginning dose in afebrile patients. In B. E., Koch's beginning dose of 0.0000025 gm.[1] should be reduced to 0.000001 gm. for afebrile and to 0.0000001 for febrile patients. This is also the dose of T. R. For B. F. the usual beginning dose may be 0.0000005 or 0.000001 cc., though in a few, especially if febrile, it may be 0.0000001 or 0.00000001 cc.

The increase of the dose depends entirely upon the individual. Haste has no place in this treatment and it is always wise to give too little rather than too much tuberculin. The usual method is to make each solution ten times the strength of the preceding and to increase the dose by tenths of a cubic centimeter. The doses should, therefore, be as follows: 0.10, 0.15, 0.20, 0.25, 0.30, 0.40 cc., etc. This will prevent the cumulative action or the hypersensibility produced by too large doses and is especially applicable in febrile patients. The dose may frequently be increased from 0.6 to 0.8 to 1 cc. of the solution without fear of a reaction.

Sahli in increasing his doses has followed a logarithmic curve. No evidence has been adduced to show that if the amount of fluid injected is never more than 1 cc. the concentration of the solution has any bearing upon the rapidity of absorption or reaction in O. T. or B. F. The greatest care in increase should be exercised in giving tenths of a milligram of O. T. or hundredths or tenths of a milligram of B. E. or B. F., as reactions most frequently occur during these doses. Once past this point without reactions, they are much less likely to occur. A large percentage (43) of patients first reacted when taking some tenths of a milligram of B. E.

The effect of small, often-repeated doses of the various tuberculins has not been sufficiently studied, although the work of Loewenstein and his assistants would suggest the danger of acquired intolerance by such a method. Wright has not noted any such tolerance with very small doses. The work of Hastings and of Kinghorn shows that, with increasing and large doses of O. T. and B. F., the negative phase of Wright does not occur, and, when it occurs, need not be considered.

It is often advised to give tuberculin every other day at first, but it is best to administer it twice a week from the beginning, for in some cases a retarded reaction occurs. When larger doses are reached or greater susceptibility is manifested, intervals of one week or longer are often advisable (for B. E. ten days or two weeks). For large, repeated doses of B. F., Denys advises an interim of seven to fifteen days. If an intermission of several weeks is required by some extraneous circumstance, it is wise to decrease somewhat the following dose.

The maximum dose to be attained in any patient varies with the individual. The relation of the size of the final dose to the benefit derived from the treatment has not been worked out. Many patients showing great susceptibility have never taken more than some hundredths of a milligram of B. E. Their after-histories differ in no way from those of individuals who attained large doses (5 mg.) without reaction. This does not hold for B. F. (Denys).

[1] B. E. and T. R.: Doses always given in solid substance of tubercle bacilli in suspension.

The extent of the pulmonary lesion or of the change in the physical signs bears no necessary relation to the tolerance, although with advancing disease or the onset of complications the tolerance is often decreased.

In B. E. 5 mg. (solid substance) should not be exceeded, while in O. T. and B. F. 1 cc. is the usual maximum dose. Denys has given 10 cc. of B. F. without ill results. The long duration of the treatment often determines the maximum dose. Some hold the dose may be increased with advantage as long as improvement continues (Sahli), but theoretically it is wiser to cease well within such limits. The maximum dose is often repeated several times.

Tuberculin administered according to these directions rarely excites any reaction until the larger doses are reached, and even then O. T. and B. F. rarely cause reaction. When a patient has once been found to be tolerant of tuberculin the increase may be more rapid and B. F., for instance, may be given in ascending doses in a scale of 0.1, 0.25, 0.5, 0.75, 1.0, until a dose of 1 or 10 mg. is reached. The increase should then be reduced. In others a scale of 0.1, 0.2, 0.4, 0.6, 0.8, 1.0 may be followed throughout. In some patients the first few doses may be 0.0000001, 0.0000005, 0.000001, and then more slowly, as suggested. Some patients in good general condition who have not previously been subjected to the tuberculin test may be begun with 0.000001 cc. of B. F. The Bacillen emulsion (B. E.) of Koch (a $\frac{1}{2}$ per cent. emulsion of tubercle bacilli) may be measured similarly as B. F., *i. e.*, by ignoring the solid contents and by taking into account only the liquid contents. The beginning dose (0.000001 solid substance) is contained in 0.0002 cc. This can also be carried out with T. R. The schema of increase for B. F. may then be followed. In any case, no matter how tolerant the patient is, the first course should be extended over five months. This can be readily done by lengthening the interval between the doses or by increasing the dose more slowly.

If at any time during the course of treatment another "brew" or a different lot of tuberculin be used, the dose should be reduced.

Tuberculin is a most powerful agent and demands the greatest care in its administration. All physicians who are not thoroughly familiar with the technique should give it most carefully and, one might almost add, fearfully. The slowest increase should be sufficient for them, and the slightest departure from the usual course on the part of the patient should be seriously considered and the dose increased or decreased accordingly. Too much stress cannot be laid upon the care that must be constantly exercised.

*Duration of Treatment.*—It is futile to expect any course of treatment extending over two or three months to be of any permanent value. No patient should be given tuberculin who cannot follow this treatment for at least five months, although shorter courses seem to be of some benefit. In the more advanced stages a longer duration is required. In most patients the focus of disease is rarely in one stage of development, and hence the need for long-continued treatment. The second and following courses of tuberculin may be given at home by the patient's physician.

The hygienic-dietetic treatment should be faithfully followed throughout the treatment. Exercise should be curtailed on the day of injection, and on the following day it is wise, especially if there be any tendency toward reaction, to keep the patient at rest in his reclining chair. The temperature should be taken before rising, and at 4 and 8 P.M., also at any time of the day if the

patient feel indisposed; in addition the weight and any unusual symptoms should be noted. If the temperature reaches 100° for more than two hours, rest in bed should be enforced until the temperature falls to normal if the reaction be slight, or for several days in cases of a severe reaction. The headache during reaction or pain at the site of injection is best treated with an ice-bag or cold applications.

The majority of patients have some manifestations of a reaction at different times during the treatment, but it is not rare, with carefully adjusted doses, for patients to escape reaction. Failure to observe the slighter symptoms of intolerance is the explanation of many failures with tuberculin. It should never be given when a patient is suffering from a coryza, an acute bronchitis, gastric disorder, fatigue or, in fact, is feeling "out of sorts" from any cause.

In most patients there comes a period of increased susceptibility when an increase in dose, which before caused no disturbance, results in a violent reaction. This period occurs most frequently when the doses of O. T. are in the tenths, of B. E. and B. F. in the hundredths and tenths of a milligram. Accordingly at this time the greatest caution should be observed. The same dose should be repeated many times if necessary, or the interval lengthened for a time. This intolerance may occur at any time if the dose be too strong or if complications arise. In most patients who have been subjected to the tuberculin test it is accentuated. By great care it can practically always be readily overcome.

At the site of injection slight redness, swelling, and soreness are not uncommon, occurring most frequently after B. E., less after O. T., and less still after B. F. Large doses of B. E. leave indurated areas, which should always be avoided on future injections, for otherwise sterile abscesses may arise. The reaction at the site of inoculation depends partly upon the volume of the dose, less upon the concentration, and chiefly upon the site, occurring least often in the subscapular region. If the symptoms are pronounced the same dose should be repeated. In all instances of a slight rise of temperature no tuberculin should be administered until the temperature has been normal or at the same level as before for two days. After a rise of temperature of 0.5° to 1° without other symptoms, the same dose at the usual interval should be given. If the temperature rise above 99.6° (in a patient with normal temperature) without other symptoms, the dose before the last should be given. With the same rise of temperature accompanied with symptoms, the next dose should be reduced to one-half to one-fifth of the last dose, or even less. When the temperature reaches 100.4° or over (rarely unaccompanied by symptoms) the dose should be similarly reduced and not given for at least a week. Tuberculin should never be given again until all symptoms produced by the last dose have completely subsided. If the symptoms were slight, an intermission of one day is sufficient; but if pronounced, at least three or four days should intervene before the next dose.

It is fallacious to suppose that the temperature when affected always rises above normal or that the maximum temperature is more sensitive than the minimum. The latter often, after slight rises of the former, falls markedly. Such a fall is present after nearly all moderate or severe reactions, and reaches its maximum on the third day or later after reaction. It may yet prove to be wise to refrain from injection until the normal minimum

is reached. This fall in the minimum seems to be more closely associated with the rise of temperature than with the injection of tuberculin.

The pulse is often quickened and at times the patient may complain of tachycardia. In such instances the interval should be lengthened and the dose reduced. Dyspnœa occurs in a number of cases, resulting from overdosage, and indicates a cessation of treatment for a time and reduction of the dose. The sputum, blood, and urine are of little aid in foretelling reaction or determining the dose. Rise of temperature is often absent when headache, pain in back or limbs, malaise, fatigue, loss of appetite, or weakness occur.

If these symptoms occur separately and are only slightly pronounced, the same dose should be repeated. If any one is severe or if several are present, the dose should be reduced. Chilliness usually indicates fever. With severe reactions various rashes may occur and enlargement of the lymph glands (axillary). In this case the following dose should then be much reduced and given at an interval of at least a week.

A continuous, even if slight, loss of weight, when below the normal, means cessation of treatment for a time at least. Care about dosage should be exercised if stimulation occur, for this is often succeeded by depression.

Symptoms of local pulmonary reaction are not often marked with carefully adjusted doses. The cough and expectoration not infrequently increase for a time and, unless severe, need not cause a reduction of the dose, although it may be wise to repeat the same dose several times. On the other hand, they may be decreased, but most frequently they remain unchanged. It is unwise to give tuberculin to a patient with acute pleuritic pain. The following dose, if the pleurisy has been severe, should be reduced. Patients with a tendency to hæmoptysis demand care in dosage. No tuberculin should be given for two weeks after an hæmoptysis of 5 to 10 cc. or more, and it is usually wise to reduce the succeeding dose. A sense of oppression in the chest may indicate cessation of treatment for a time, then reduction of the dose and careful increase.

The relation of the increase of physical signs to the dosage has not been fully worked out. Marked changes do not usually occur until large doses are reached, and even then are far from constant. It is a wise proceeding to repeat the same dose until marked evidence of increase of physical signs is no longer present. An increase of dose, however, during this time seems to do no harm.

In brief, a patient may be said to be doing well when the temperature and pulse rate remain normal (except occasionally for one or two days following injection), when the weight is maintained at normal, when the general condition, the appetite, and the color of the skin are all good, and when the pulmonary symptoms are decreasing. If, on the contrary, the temperature of the patient be elevated for many days, the pulse rapid, and there be loss of weight, appetite, slight cyanosis, increase of the pulmonary symptoms, due possibly to secondary infection (influenza, etc.), or repeated hæmoptysis, cessation of the treatment for a longer or shorter period is imperative.

This method of using tuberculin is based solely upon clinical experience, and the effect of any one dose cannot be accurately estimated. So far no practical method has been discovered by which the effect of each dose can be followed and the succeeding dose properly estimated. Many reactions can, however, be avoided by careful clinical observation. The patients should be taught to record accurately any symptoms, however slight. Even

the most pronounced neurasthenic patients, if given tuberculin, betray no increased nervousness on account of keeping such a record, and, at least in the writer's experience, often less.

*The Effect of Repeated Tuberculin Injections.*—Tuberculin in sufficient doses causes a congestion of the tuberculous foci, long thought necessary for healing, although recently doubt has been thrown upon it by the work of Wright. The local (organ) reactions in patients with mixed infection following large doses may result in great harm. Large doses of tuberculin are said to cause increased fibrosis about the tuberculous foci and elsewhere.

Injection of tuberculin causes the formation in the serum of antituberculin bodies (Arloing), although many have been unable to demonstrate them. B. E. causes marked increase of the agglutinins for tubercle bacilli. Arneth, through a study of the nuclei of the polymorphonuclear leukocytes, concluded that the blood pictures becomes more nearly normal. Lupton and Brown found a slight increase in the leukocytes, which only in the rarest instances, however, reached 10,000 per cmm.

The sputum is increased at first and may be more purulent. Later it often decreases or ceases. The tubercle bacilli really increase in numbers at first, only apparently later as the sputum decreases. Their form and virulence undergo little if any change, but clumping is said to be more frequent. Denys and Buchanan have noted increased phagocytosis, Allen a marked diminution. Tubercle bacilli disappear more frequently from the sputum in treated patients.

The writer's notice has repeatedly been called to the fact that many patients, treated with tuberculin, deserving apparently a poor prognosis, have enjoyed freedom from febrile attacks and escaped complications, apparently more often than the non-treated patients.

**The "Opsonic" Theory.**—Wright, with Leishman and Douglas, has revived Metchnikoff's idea of the value of phagocytosis in immunity. While marvellous results have been accomplished in many infections, the task in tuberculosis is more difficult, and probably only the earliest stages of pulmonary tuberculosis may be successfully treated. In advanced pulmonary tuberculosis the index fluctuates widely, ranging from even 0.3 to 1.8 or higher (normal variations 0.8 to 1.2).

Crace-Calvert sums up the results in pulmonary tuberculosis as follows:

1. In slight early cases the index appears to be above normal.
2. In acute cases the index fluctuates greatly from day to day.
3. In chronic cases the index appears to be below normal.
4. In sanatorium "cures" the index appears to be variable.

From this it would appear that the only cases to be benefited are those classed as "chronic" and possibly some early cases whose index is low.

In their work Wright and his followers have employed tuberculin R or an emulsion of tubercle bacilli heated on three successive days to 60° C. only. The dose employed has ranged between $\frac{1}{1000}$ and $\frac{1}{500}$ mg. of the solid substance. They have not found it necessary to increase the dose, and it is timed by following the opsonic-index curve. The injection is usually made when, after a rise, the curve begins to fall.

**Treatment with Bacteria.**—Many living bacteria have been used in the treatment of tuberculosis. Human tubercle bacilli have been employed with marked success in cattle (Pearson and Gilliland, v. Behring, McFaydean). The attenuated forms markedly prolong the life of guinea-pigs. However,

the time has not yet come when tubercle bacilli attenuated by any means can be recommended in man, although Moeller, after vaccinating himself with human tubercle bacilli, passed through a slow worm, inoculated himself with virulent bovine tubercle bacilli and had no untoward results.

Inoculations of acid-fast bacilli have little effect other than causing agglutination of tubercle bacilli. Many bacteria have been used, streptococci (from erysipelas), streptothrix, *B. coli*, *B. tumescens*, *B. mesentericus*, and yeast, rich in nuclein, has been used by Fournier and Huggard. The results are unsatisfactory.

Vaccination with the secondary organisms has been used by Denys and Wright. The serous exudate of blisters has been used as a specific by Mangant, and others (Flick, etc.) have advocated the production of blisters, protecting them carefully in order to allow the contents to be re-absorbed.

**Serotherapy.**—Antitoxic serums have met with little success. Trudeau and Baldwin could obtain no evidence of any antitoxic properties in the serum of the horse, ass, cow, chicken, and rabbit treated with tuberculin. Other observers, especially Maragliano, Marmorek, and de Schweinitz, report favorable results. Maragliano's serum has proved at the Phipps Institute, and in a few instances at Saranac Lake, to be of little or no value. The recent work of Pirquet, Schick, Rosenau, etc., has shown that, in small doses at long intervals, serum may be very dangerous. The injection of normal serums has yielded no benefit. Marmorek has recently suggested the use of serum per rectum, claiming for this method much less constitutional disturbance.

**Organotherapy.**—The extracts of the lymphatic glands or the powdered glands have been given, but without marked success. Long-continued ingestion of virulent tubercle bacilli by leukocytes (of sheep) *in vitro* renders them avirulent, non-chemotactic, and unable to proliferate, according to Bartel, but still capable of producing active immunization. This observation if confirmed, coupled with Wright's "opsonic" experiments, is very suggestive. Bartel hopes to produce an antitoxic substance in animals treated by this method.

**Hydrotherapy.**—This helps in withstanding cold (hardening process), strengthens the heart, slows the pulse, increases the vasomotor tone of the cutaneous bloodvessels (and so raises the blood pressure), often aids the appetite and causes deeper breaths to be taken. Its effect upon the nutrition and secretion of the skin is marked. Great freedom from colds is enjoyed by many patients who follow these methods—a most important point.

Every patient with pulmonary tuberculosis should take daily, preferably on arising, a cold bath. After drying himself, he should experience a glow, a feeling of warmth, produced by the dilatation of the cutaneous vessels, following the primary contraction caused by the cold. In other words, he should react. Should this not occur or should heart disease, aneurism, marked arteriosclerosis be present, it is wise to abandon any vigorous hydropathic measures.

For patients who fail to react and for all patients susceptible to cold, it is wise at the beginning to insist upon a few simple measures. The bath should always be taken in a warm room (never below 55°). The lower half of the body may be clothed. All cleansing should be done with warm water (100°) and the cold (40° to 60°) should be applied with a sponge to the neck, chest (front and back), and arms as quickly as possible (about one

to two minutes), and immediately dried. It may be necessary to begin the sponging with tepid water (80° to 100°) after the warm (100° to 110°), and gradually from day to day to reduce the temperature. In other cases it is best to begin with sponging one arm, then on the following day both arms, and so on until the body to the waist has been sponged. Alcohol rubs may have to be substituted for a time.

For more vigorous patients, especially those long accustomed to it, the instantaneous cold plunge (50° to 70°) may be permitted. Others prefer a cold shower or full cold sponge, standing meanwhile in warm water. For many patients, however, these are not advisable, especially in winter, unless the water is slightly heated. In some patients nervousness is increased by too cold baths. Twice each week every patient should take a warm (100° to 105°) cleansing bath, using soap freely. This should be followed by a cold sponge or spray and the water never cooled gradually.

Hydrotherapeutic measures directed against the fever have helped little in pulmonary tuberculosis. Every patient with fever and confined strictly to bed should be given each night a brine bath (sea-salt ℥ss in water Oij), the temperature of which should be gradually lowered, but never so low that a reaction fails to follow. An alcohol rub may be given afterward. In the morning a cold sponge to the waist or an alcohol rub should be given.

The "cross-binder" worn during the night may be of help in severe cough with tenacious sputum, for pain in the chest (pleurisy, etc.), for catarrhal conditions of the upper air passages, and for insomnia. Winternitz recommends it during the day for fever, with the use of a water coil morning and afternoon. A strip of cotton cloth of several thicknesses, three to four inches wide and twenty to twenty-four inches long, dipped in cold water, should pass over each apex and be held in place by a piece of similar cloth, six to nine inches wide, encircling the chest. These should be covered with a flannel bandage, snugly applied, three inches wide. Oiled paper, muslin, or silk may be used under the flannel bandage, but is not necessary. When removed in the morning the chest should immediately be sponged with cold water. A few patients fail to react to the cross-binder, and they should be rubbed, with or without alcohol, until warm, before it is applied.

**Pneumotherapy.**—The value of pneumotherapy is doubtful. The breathing of compressed air is distinctly dangerous to patients with pulmonary tuberculosis.

**Inhalations.**—No substance has yet been found (nor will it be) that acts only upon the diseased parts of the lung. Another and graver objection to inhalations is the difficulty the substances experience in gaining admission to the deeper parts of the lung. The secretions upon the surface of the air passages may be coagulated by or may absorb the inhalant. Then the diseased areas are often impermeable, and, if permeable, the lesion may still be closed. From these facts it is readily seen that no "specific" introduced by inhalation and acting directly upon the focus of disease can be hoped for.

Inhalations are, however, of marked benefit in some cases, especially when complications of the upper respiratory tract occur. Another important fact is the usually very moderate but necessary respiratory exercise which they entail. It is difficult to say what parts of the results are due to this factor and what to the inhalation *per se*.

**Injections.**—A large number of substances have been injected into the body per rectum, subcutaneously, intravenously, intratracheally, and into

the pulmonary tissue. None of these are of great value. Some intratracheal injections (camphor, menthol, etc.) aid in the control of cough.

**Electricity and Light.**—Static electricity has been recommended, but has been little used. The *x*-rays are of no value, dangerous on account of burns, and some believe harmful through spreading the disease. The high-frequency currents have been more frequently employed. They should not be employed in weak patients and may produce hæmoptysis. The recent use made by Finsen in lupus of the actinic rays has again brought into notice the sun baths of the ancient Greeks. Apparently much used in the Riviera, they are said to be especially beneficial to neurasthenic patients.

**Surgical Treatment.**—The early excision of the tuberculous focus has been frequently discussed and several times attempted, once or twice successfully, but the most careful examination fails to indicate whether the disease exists in one or many areas.

The early calcification of the first costal cartilage, resulting in lessened movement and narrowed apical aperture, led to the suggestion that in early stages an artificial joint be produced by cutting through the first costal cartilage. It has met with little favor. Numerous observers have advocated that the diseased lung should be put at rest, by strapping the chest, by the injection of air, simple or carbolized, filtered or unfiltered, or of nitrogen gas. These methods have little to recommend them and are not unattended by danger.

The surgical treatment of tuberculous cavities has produced few favorable results. The excision of one or several ribs over a tuberculous cavity has been advocated for healing and for relief of symptoms. Except in gangrene it is doubtful if pneumotomy is ever of much benefit.

**Accessories for Treatment.**—The articles necessary for comfort while out-of-doors vary greatly according to climate, season, and individuality. It has been deemed wise to refer briefly to some of the appliances found to be of value after practical use. Inasmuch as in summer few or no wraps are required, this section will deal largely with the requirements needed in a cold climate, where, even when the thermometer falls below zero, the cold can be comfortably defied. A most important factor is that patients who undergo the outdoor treatment must live from six to ten or more hours in the open air. For this reason it is foolish to fit up a room luxuriously and neglect the porch, veranda, or wherever the patient passes his time out-of-doors. No detail, no bearable expense, should be omitted to make the porch comfortable.

Few climates are so perfect that protection against wind, rain, snow, or sun need not be afforded. Accordingly, Liegehalle, revolving shelters, shacks, huts, garden-houses, porches, roofs, fire-escapes, have all been used. The porch, preferably facing south in winter, north in summer, should be roomy, well protected by a roof and glass screens on one or possibly two sides, but never on three. The depth should be little greater than the height of the roof in front. It should be well lighted by electricity. Awnings may be used during summer. When occupied by more than one patient it should be so spacious that the chairs can be at least four feet apart.

A strong, comfortable, roomy, long, broad-armed chair, with a movable high back, provided with a good mattress and pillows with washable covers, and with a book rest or reading table, is a *sine qua non*. No chair is more

comfortable than Dettweiler's, but the Adirondack Recliner is as comfortable and very much more durable. Metal chairs last little longer and are very heavy. A light wooden chair with a canvas seat can be obtained cheaply and is very serviceable. Swinging chairs are less desirable, as the position is too readily changed. Hammocks constrict the shoulders. A wheel chair is excellent during convalescence from an acute exacerbation.

In cold climates a fur coat, with a collar reaching above the ears, is a necessity, while fur rugs are more or less of a luxury. Steamer rugs are excellent, but horse or ordinary blankets and quilts answer every purpose. Sleeping bags are comfortable and should be made to come up to the armpits, front and back, opening in some cases down the front. Foot muffs lend great protection to the feet. A small table for the sputum cup, bell, books, writing materials, etc., is very important. On exposed verandas wind shields are necessary. Foot warmers (soapstones, hot bricks, hot-water cans, electric contrivances) should, on account of chilblains, be avoided, if possible. Weak patients should never be allowed to wrap themselves up.

Cardigan jackets are much better than sweaters and chamois waistcoats. A sash about the waist outside the fur coat is helpful. Gloves or mittens of fur or pure wool, extending over the cuff of the coat, are required. Wind guards in the sleeves add much warmth. Woollen stockings, with or without lisle-thread stockings under them, loose shoes with flexible soles, felt shoes, moccasins, leather or woollen leggings, equestrian tights (for women), lumberman's felt boots reaching to the knee ("Pontiacs"), may be tried successively for cold extremities. The head may be bare or covered with a toque or with a fur or wool cap, protecting the ears and the eyes (by a visor).

**For Patients Confined to Bed.**—The room, at least 10 x 12 feet, should have two windows, preferably in adjoining sides, reaching nearly to the ceiling (10 feet high). All ledges and corners should be avoided and the wall covered with washable paper or paint. The waxed floors, preferably of hard wood, may be covered with linoleum. Only one or two small rugs are advisable. All furniture should be well raised from the floor and, if upholstered, covered with leather or washable covers. Electric light and hot water or low pressure steam heating should be used. Fireplaces, on account of dust, are objected to by some, but it is to be remembered that the rooms must be habitable and, for this reason, the exclusion of fireplaces and a few plainly framed pictures savors of hygiene run mad. Coal-oil stoves should be avoided. Washable curtains, ending six inches above the floor, are not objectionable.

Opening out of one window which extends to the floor should be a porch, so arranged that the bed, wheeled out upon it, is fully protected from rain, wind, or snow. When for various reasons the windows cannot be sufficiently opened, "window tents," now in use for some years, may be tried. A sense of constriction, due to the nearness of the walls, is constantly present, and the value of these appliances has not yet been thoroughly established. Long tubes extending from the window to the patient's bed should be avoided.

The bed should be of iron with a mattress of hair, air, or water. It should never occupy a corner nor stand with its head in a draught. A thin gauze screen placed in a window, which should not be closed, will often prevent

a draught. A movable back-rest is important for the treatment of hæmoptysis, expectoration, dyspnœa, and for eating, especially when change of position produces violent coughing. A small bedside table for the cup, bell, urinal, etc., and a bed table, extending over the lap of the patient, to be used when eating, reading, etc., are important.

Many good nurses are of little help in pulmonary tuberculosis. Great tact and cheerfulness, constant watchfulness, much ingenuity, both in mental suggestion and the preparation of food, are necessary. In many cases the success of the battle lies in the hands of the nurse. When she begins to flag or waver, as is to be expected in so chronic a disease, a change should be at once made.

**For Patients Sleeping Out-of-doors.**—When possible the bed should remain indoors until the patient is ready to retire, or, if possible, it should be heated with hot-water bottles, which, if well wrapped up, can be pushed to one side and remain warm for some time Two mattresses, one preferably a box mattress, with paper between them; three to five pairs of double blankets, with a mackintosh sheet over them (protection against rain, etc.), or with a fiber blanket between them; a lamb's-wool quilt and flannel or outing flannel sheets are all useful. The pillows should be arranged in the form of a V, with the apex at the head of the bed to receive the head of the patient, or, better still, three pillows should be used, one extending down either side, parallel to the body, and a third for the head. Some patients prefer to tuck the covers under them and so form a sleeping bag. Such bags may be used. On very cold nights it is wise to cover the pillow or bed-clothes with a half-dozen small flannel squares, which can be removed one at a time when the breath freezes upon it, and to cover the face with cold cream or vaselin. Woollen or outing flannel night garments, a cardigan jacket, sweater or bath robe, a woollen hood covering the ears and extending down under the jacket, a domino mask (lined with flannel), bed-slippers, "boots" of flannel, are all used.

**Euthanasia.**—When, after consultation with one or more physicians, it has been decided that all hope for recovery is past, and that three or four months of existence may elapse before death, it is in many cases kinder not to relax apparently any efforts directed toward overcoming the disease, but after some slight opposition, if need be, to acquiesce to the patient's wishes. Care should be exercised not to begin the hypodermic injection of morphine too soon, for fear it may lose its effect. Small doses (gr. $\frac{1}{16}$) night and morning lessen the dyspnœa, check somewhat the cough, and greatly improve the general comfort of the patient. The dose should be slowly increased. Inhalations of oxygen often give the greatest relief and should always be used for trying dyspnœa.

**Results.**—The results in general are most encouraging. In the mind of the laity the former pessimistic view is gradually waning, and in many instances is replaced by the belief that every case of tuberculosis is curable. Some physicians of wide experience even go so far as to say that every case of non-acute pure pulmonary tuberculosis is curable. Neither of these statements can stand in the light of our present knowledge. It is an easy task so to improve the general condition of a patient as to give him all the outward appearances of health, but it is a far different task to get him into such a general and pulmonary condition that after a few months at work he will not relapse.

Pulmonary tuberculosis is a relapsing disease. The results must therefore be considered under two heads, immediate and ultimate. The immediate results may be manipulated, even unconsciously, but the test of time is rigorous and "living" and "dead" admit of no personal equation or variation of definition. The immediate results are difficult to handle and comparison of these from different sanatoriums, on account of the lack of uniformity, has up to this time been impossible or at least of little value.

**Classification.**—Patients must be classified on admission, on discharge, and according to the ultimate results. A classification should take into account not only the amount of disease in the lungs, but the actual condition of the patient. It must consider symptoms as well as the pathological and general conditions, for no one alone is sufficient. The personal equation should be eliminated as far as possible. The divisions, or classes, should be as sharply separated as possible and not too numerous, three being the number most widely advocated for many years. Prognosis and classification are closely associated.

The classifications used may be said to be based (1) upon the pathological conditions in the lungs, (2) upon one or more symptoms, or (3) upon the pathology, the symptomatology, and the general condition. Most classifications have been based upon the pathological process in the lungs, *e. g.*, (I) Fibrosis, (II) Colliquative necrosis; or (I) Infiltration, (II) Consolidation, (III) Cavity formation.

Turban classifies patients wholly upon the physical findings, which changing as they do, and occurring with such different symptoms, render this far from accurate in portraying in what real stage of the disease any patient may be—a point he early acknowledged. By this classification, Stage I includes those patients whose slight lesion does not exceed one lobe or two half-lobes. Stage II includes those whose slight lesion extends farther than Stage I, but at most to two lobes or a severe lesion extending at most to the volume of one lobe. Under Stage III are all not under I and II. "Slight lesion" is synonymous with infiltration and "severe lesion" with consolidation and excavation. Purely pleuritic dulness of slight extent is left out of account. Slight alterations in the breath sounds, *e. g.*, harsh breathing or prolonged expiration without change in percussion and without rales, are not to be considered. This properly balances both the extent and the intensity of the pathological changes, two factors, one of which is ignored in most anatomical classifications.

Few classifications have recently been founded purely upon symptoms. The best classification so far suggested is that adopted by the National Association for the Prevention and Study of Tuberculosis, and based largely upon Trudeau's and not upon Turban's. The incipient stage is very narrowly defined, in the hope of encouraging early diagnosis. The "moderately advanced" stage includes patients who differ much more widely among themselves than some in its ranks differ from those in the incipient stage. The exact amount of involvement is not stated, but any patient with signs extending below the second rib should be classified as moderately advanced. The classification is as follows:

*Incipient* (*Favorable*).

Slight initial lesion in the form of infiltration limited to the apices or a small part of one lobe.

No tuberculous complications. Slight or no constitutional symptoms

(particularly including gastric or intestinal disturbances or rapid loss of weight).

Slight or no elevation of temperature or acceleration of pulse at any time during the twenty-four hours, especially after rest.

Expectoration usually small in amount or absent.

Tubercle bacilli may be present or absent.

*Moderately Advanced.*

No marked impairment of function, either local or constitutional.

Localized consolidation moderate in extent, with little or no evidence of destruction of tissue; or, disseminated fibroid deposits. No serious complications.

*Far Advanced.*

Marked impairment of function, local and constitutional.

Localized consolidation intense; or, disseminated areas of softening; or, serious complications.

*Acute Miliary Tuberculosis.*

Greater diversity of opinion and of usage exists in the classification on discharge than on entrance, and the National Association has slightly modified Trudeau's classification as follows:

*Progressive* (Unimproved).—All essential symptoms and signs unabated or increased.

*Improved.*—Constitutional symptoms lessened or entirely absent; physical signs improved or unchanged; cough and expectoration with bacilli usually present.

*Arrested.*—Absence of all constitutional symptoms; expectoration and bacilli may or may not be present; physical signs stationary or retrogressive; the foregoing conditions to have existed for at least *two* months.[1]

*Apparently Cured.*—All constitutional symptoms and expectoration with bacilli absent for a period of *three* months; the physical signs to be those of a healed lesion.

The use of tuberculin as a test of cure has been suggested by many observers. The results obtained in this way and by clinical methods do not agree, as many patients clinically "apparently cured" react to tuberculin. Nagel discharged 114 of 183 patients as clinically cured, and of these 114 patients (38 per cent.) reacted to tuberculin. Careful clinical observations determine sufficiently accurately whether or not a patient is "apparently cured."

**Ultimate Results.**—The real test is the division of all patients into two classes—living and dead. The division of the first class is difficult. Here ability to work is of most value, for it is difficult to obtain a physician's report on the general or pulmonary condition or on the sputum examination. The National Association for the Study and Prevention of Tuberculosis defines "cured" as follows: All constitutional symptoms and expectoration, with bacilli absent for a period of two years under ordinary conditions of life. An absolute cure can only be determined after death. At the Adirondack Cottage Sanitarium it is impossible to use this term "cured," for sufficient information cannot be obtained, and "well" has been substituted.

[1] The length of time mentioned is of course somewhat arbitrary, but is intended to cover the cases which frequently occur, where the patients leave a sanatorium for various reasons, contrary to advice, after a stay of a few weeks, although all active symptoms may have ceased completely soon after entrance.

**Statistical Reports.**—The best statistical report is the one suggested by Turban, with the modifications adopted by the National Association. These consist in giving the side or sides of the lesion, full data on discharge as well as on admission, and the figures for temperature, pulse, and respiration, instead of symbols. To collect a mass of statistics which will be of value, the Association further suggested that each sanatorium publish in its annual report the tabulation for each patient.

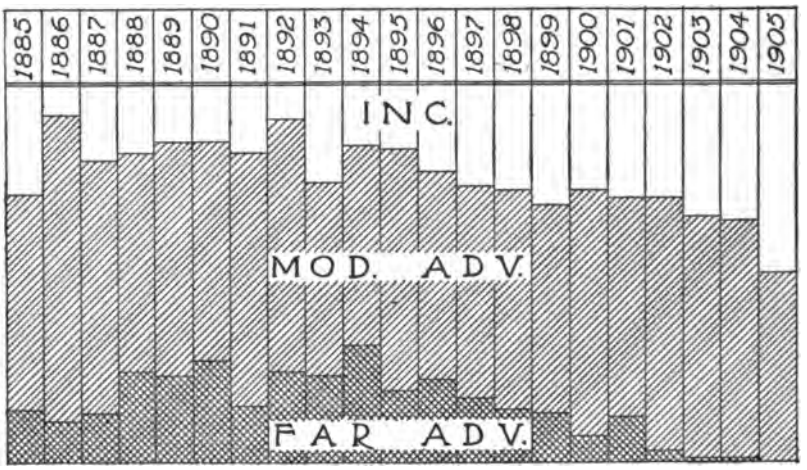
**Results of Dispensary Treatment.**—These are difficult to estimate. Many of the patients in early stages are sent at once to sanatoriums, some in more advanced stages go to hospitals, and the majority who undergo treatment at the dispensary are under more or less unfavorable surroundings. The true results of the dispensary can never be shown by statistics.

**Results in Sanatoriums.**—The results of modern treatment are necessarily based upon the results obtained in sanatoriums, for results obtained outside of these institutions are seldom if ever given in sufficient detail to be of value. This also applies to the results at many sanatoriums which, started under adverse financial conditions, have published no report or given too meagre details to be of much value. Few sanatoriums, especially in America, have been in existence long enough to make the ultimate results of treatment very valuable. The time of residence in the sanatorium is of much importance for the results.

*Results at the Adirondack Cottage Sanitarium.*—A study of the results obtained shows at once the great value of early diagnosis in both immediate and ultimate results. Although the patients in the incipient stage were less than 28 per cent. of the total number, yet they furnished 69 per cent. of those apparently cured on discharge. Of patients in the incipient stage 14 per cent. are dead, while of those in the moderately advanced 43 per cent. and of those far advanced 81 per cent. are dead. Of the patients in the incipient stage discharged with active disease (*i. e.*, neither apparently cured nor arrested) five times as many recover, more than twice as many are alive, and only one-fourth as many are dead as those discharged with active disease in the moderately advanced stage. Of all patients admitted in a far-advanced stage only 3 per cent. are alive and 1 per cent. are well. To enable one to grasp more readily these statistics from the Adirondack Cottage Sanitarium, a number of diagrams have been constructed. The condition of the patients on admission is graphically shown in Fig. 13. The immediate results are graphically shown in Figs. 14 and 15. The incipient and moderately advanced stages are shown separately, for the results vary so widely that they cannot really be discussed together. In Fig. 14 the number of apparently cured patients has markedly decreased since 1902, owing to the fact that much more rigorous examinations of both patients and sputum have been made since that time. The effect upon the moderately advanced patients, Fig. 15, is less apparent, but the increase of those discharged with arrest is much greater since 1892, which is possibly due to the greater restrictions put upon those with active disease. In other words, the rest cure has been more rigorously enforced. In Figs. 16, 17 and 18 the percentages of living and dead are graphically shown; the dotted line is approximately the normal death-rate curve. In Fig. 16 the ultimate results for all patients are shown. On the whole, the death rate for the apparently cured patients may be said to be double the general death rate. For patients discharged with arrested disease the death rate may be said to be eight times the general death rate.

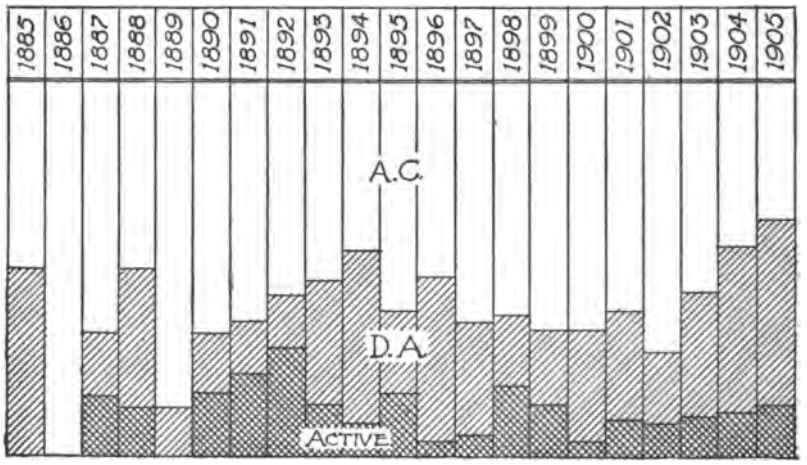
The patients who were neither apparently cured nor arrested on discharge may be said to have on the whole a death rate twenty-eight times the general death rate. In Fig. 17 all patients with active disease on discharge have

FIG. 13




Conditions on admission, expressed proportionately, of patients discharged each year from the Adirondack Cottage Sanitarium.

FIG. 14

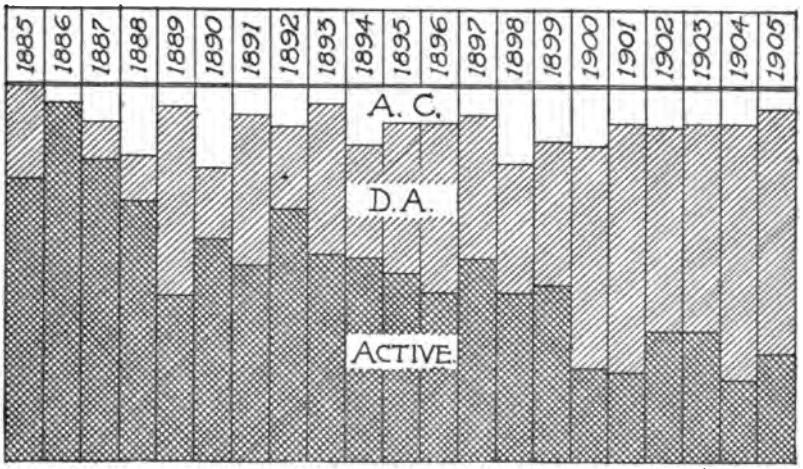



Conditions on discharge, expressed proportionately, of patients in the incipient stage, discharged each year from the Adirondack Cottage Sanitarium.

been omitted. Classifying the patients by condition on admission, patients in the incipient stage do vastly better than those in a moderately advanced stage. Roughly, over 50 per cent. of the patients in the incipient stage are

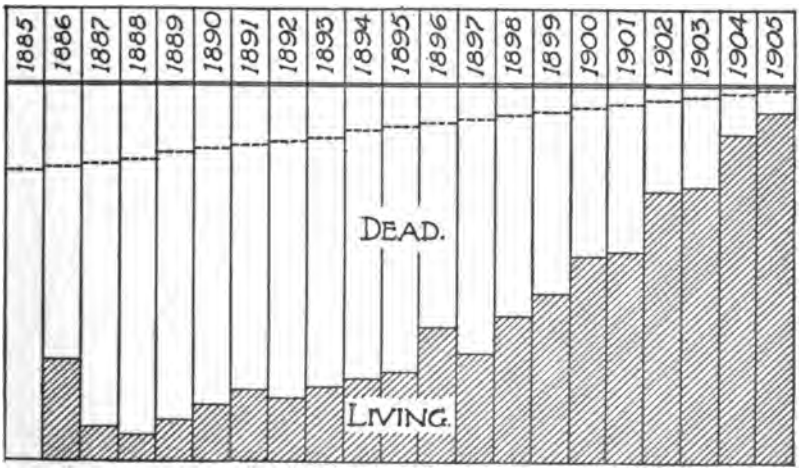
alive fifteen years after discharge, while about 50 per cent. of those with moderately advanced disease are dead in six years. The classification by condition on discharge shows even a more striking picture. In Fig. 18 the

FIG. 15




Conditions on discharge, expressed proportionately, of patients in moderately advanced stage, discharged each year from the Adirondack Cottage Sanitarium.

FIG. 16

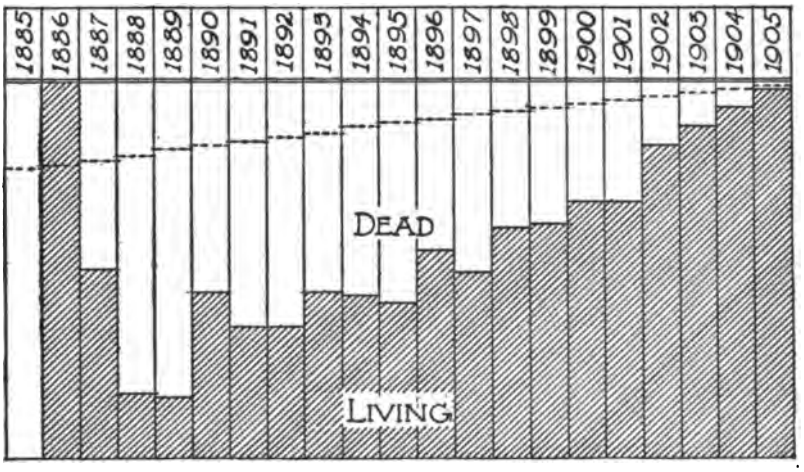



Proportions of the dead and living in 1906 of all those discharged in each year from the Adirondack Cottage Sanitarium. The broken line shows the proportions (above dead, below living) according to a general mortality table (Farr, No. 3).

ultimate results in those discharged apparently cured are seen to approximate rather closely, the normal death-rate curve proving that the term "apparently cured" is really justified and should not be replaced by "arrest,"

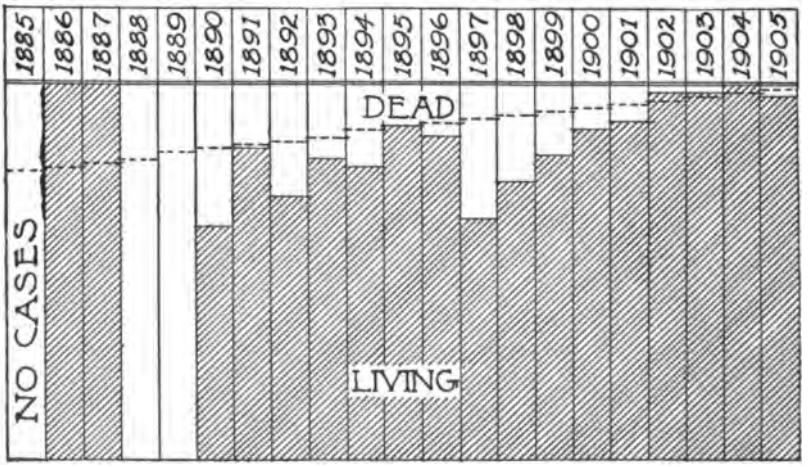
as some would have it. The results in those discharged with arrested disease are far less encouraging. In six years over 50 per cent. are dead.

FIG. 17




Proportions of the dead and living in 1906 of those discharged apparently cured and arrested in each year from the Adirondack Cottage Sanitarium. The broken line shows the proportions (above dead, below living), according to a general mortality table (Farr, No. 3).

FIG. 18




Proportions of dead and living in 1906 of those discharged apparently cured in each year from the Adirondack Cottage Sanitarium. The broken line shows the proportions (above dead, below living), according to a general mortality table (Farr, No. 3).

*Loss of Tubercle Bacilli in the Sputum.*—Only about 40 per cent. of all patients with tubercle bacilli in their sputum on admission lose them during sanatorium residence—a fact long ago pointed out by Koch. Of 962

patients at the Adirondack Cottage Sanitarium, 354 had no tubercle bacilli in the sputum on admission. Of 608, 244 (40 per cent.) lost them during residence. Division of these patients into groups with residence under and over six months shows that of the former 34 per cent. and of the latter 43 per cent. lose their bacilli. The value of the longer term of sanatorium residence is readily seen.

*Loss of Physical Signs.*—Complete disappearance of the physical signs is rarely attained, although Reiche among 1571 found 118 cases. Among 2225 patients at the Adirondack Cottage Sanitarium, 59 lost all their physical signs. Of these, 41 were in an incipient and 18 in an advanced stage. Of the latter, 13 are living, 1 is dead, and 4 untraced; of the former, 34 are living, 1 is dead, and 6 untraced. Complete loss of physical signs has, therefore, great bearing upon the ultimate results.

*Weight.*—The effect of sanatorium treatment upon the weight is strikingly shown in a study of 901 patients (453 males, 448 females) at the Adirondack Cottage Sanitarium. The weight of the men on arrival in the Adirondacks was 90 per cent. of their standard weight, that of women 91 per cent.; on discharge the men weighed 99 per cent. and the women 102 per cent. of this standard weight. Their usual weight in health was for the men 94 per cent. and for the women 95 per cent. of the true normal.

*The Results in German Sanatoriums.*—The results obtained at the sanatoriums founded largely by the German insurance companies are very striking when compared with the results obtained in all other diseases. The patients with pulmonary tuberculosis do slightly better the first and second years after discharge, nearly as well during the third year, while there is a decided advantage in favor of the non-tuberculous patients, which might be expressed as 6 to 5, during the fifth year after discharge. The women do decidedly better than the men and the difference between the tuberculous and non-tuberculous patients is much less, due some hold to the less strenuous struggle for existence many of them lead. All relapsed patients are not re-admitted, and, while the proportion refused is not stated, the figures would seem to indicate that fewer non-tuberculous patients relapse after the first year.

The results obtained by the insurance sanatoriums of the Hanseatic League have been much quoted. Of 4822 patients treated, 69 per cent. are able to work, 12 per cent. are pensioned, and 20 per cent. are dead from one to ten years after discharge. The percentage of pensioners remains remarkably even (this covers the class "living" in the Adirondack Cottage Sanitarium reports). Not until between eight and nine years after discharge are 50 per cent. of the patients dead, and at the end of seven years 66 per cent. of the patients are still capable of work. These are the best results so far obtained covering a large number of patients. A large percentage of these patients had closed tuberculosis and were diagnosed by the tuberculin test.

A study of 6000 patients, collected by the Imperial Board of Health (Berlin) from different German sanatoriums up to 1901, showed that of every 100 patients there were, on discharge: 67.3 thoroughly capable of resuming their former calling; 7.1 thoroughly capable of engaging in another calling; 14.6 partly capable of work; 11.0 incapable of work; 87.7 were discharged as cured or improved; 8.8 as unimproved; 3.1 as worse; 0.5 died.

*Children.*—The results of sanatorium treatment in children are excellent. The figures of Moeller at Belzig show that in comparison with 960 adults a much larger proportion of 161 childen are healed, fewer improved or remained unchanged, but none died, while a small percentage of the adults did. More children than adults in the third stage of Turban fail. A comparison of 43 children and 170 women at Stoney Wold Sanatorium shows that children in incipient and moderately advanced stages do far better than adults, while those in far-advanced stages do worse (a matter of slight importance). King, at the Loomis Sanatorium, obtains similar results.

**Results of Tuberculin Treatment.**—No scientific basis for the very optimistic view of the tuberculin treatment that is at present widely gaining ground can be found in the vast majority of the results so far published. The figures seem to indicate that tuberculin treatment is of value and the vast majority of all who have used this treatment are in favor of it, while admitting in some instances the discrepancy between their opinions and their figures. Many writers upon the tuberculin treatment have grouped all classes of patients together and hoped to get thus an idea of the results of tuberculin treatment. Such methods easily lead to false conclusions. When patients are carefully classified on admission the divisions of the classification may be so broad that such selection can be exercised as to interfere gravely with comparison of patients. Few published statistics escape the error of selection.

*Results of Tuberculin Treatment at the Adirondack Cottage Sanitarium.*—Trudeau began the use of tuberculin at the Adirondack Cottage Sanitarium in 1890, and notwithstanding much opposition for many years has employed it ever since. The patients treated with tuberculin were carefully selected; few doing exceptionally well were chosen, but all had tubercle bacilli in their sputum until 1902, when tuberculin was administered to any patient who wished it and who presented no serious complication or fever. More recently slight fever has been looked upon as no contra-indication. Koch's original tuberculin, his bacillary emulsion, Trudeau's modification B, Denys' bouillon filtrate, and tuberculo-plasmin have been chiefly used, while tuberculin R and tuberculol have been given to a few patients. At first tuberculin was given to a few patients with far-advanced disease, in some instances as a last resort. All the patients in this stage are dead. From 1897 to 1900 a large percentage of patients in the incipient stage were given tuberculin, and during 1903 and 1904 none of that class received it. The moderately advanced class has always been the most largely represented.

The actual comparison of results is difficult, as the standards and number of patients treated have varied from year to year, but by reducing (or increasing) the numbers of treated and untreated for each year to 100 in each class the influence of varying numbers is eliminated. A study of 185 patients treated with tuberculin and 864 not so treated, all of whom stayed over ninety days and had tubercle bacilli in their sputum on admission, shows for the incipient stage a slight difference on discharge in favor of the treated patients. For the moderately advanced stage a very marked difference on discharge in favor of the treated patients is observed (apparently cured, treated 27 per cent., untreated 6 per cent.; disease arrested, treated 50 per cent., untreated 51 per cent.; active, treated 18 per cent., untreated 43 per cent.).

The ultimate results obtained from one to fifteen years after discharge

in 135 patients treated and 690 untreated, all of whom stayed over ninety days and had tubercle bacilli in their sputum, show that of 100 patients in the incipient stage treated with tuberculin 79 are alive, of the untreated 63 are alive, while in the advanced stage 61 of the treated patients are alive and 36 of the untreated.

**Loss of Tubercle Bacilli.**—Of all patients with tubercle bacilli in their sputum who undergo sanatorium treatment, only about 42 per cent. lose them. Any factor that can be introduced into sanatorium treatment to increase this figure is of great importance. Accordingly, if it could be shown that tuberculin caused the disappearance of tubercle bacilli in a greater number of patients, its value would be unquestionable, even if it did little else. The disappearance of tubercle bacilli from the sputum depends directly upon the length of sanatorium residence. Tuberculin treatment can rarely be completed under five months, and in most institutions the patients receiving tuberculin remain on the average longer than the untreated. At the Adirondack Cottage Sanitarium the average residence for patients so treated was considerably longer than for the untreated. The care and accuracy with which the sputum is examined, as well as the frequency, has much to do with these result at the Adirondack Cottage Sanitarium. Kreuser selected 110 patients with tubercle bacilli in their sputum and treated 55 without and 55 with tuberculin. Of the latter 22 lost their bacilli, of the former 16. Philippi compared 98 patients without tuberculin treatment with 28 so treated (all afebrile), and found in the second stage (Turban) 19 per cent. of the untreated and 58 per cent. of the treated lost the tubercle bacilli from their sputum, while of the third stage 7 per cent. of the untreated and 31 per cent. of the treated lost their bacilli. Turban found at the end of from two to six years that 48 per cent. of the treated and 27 per cent. of the untreated had sputum free from tubercle bacilli.

The treatment of pulmonary tuberculosis with tuberculin may therefore be said to be of value. It is of more permanent benefit to patients in moderately advanced than in incipient stages, and of slight if any value for those with far-advanced disease. The general nutrition of patients is little affected, but more lose their tubercle bacilli.

The writer acknowledges his indebtedness to Mr. E. G. Pope for many of the statistics as well as for many suggestions in all sections of this article.

# CHAPTER XII.

## SYPHILIS.

By WILLIAM OSLER, M.D.,

AND

JOHN W. CHURCHMAN, M.D.

**Synonyms.**—Lues venerea; bad disorder; pox; morbus gallicus; French, vérole; German, Lustseuche; Krankheit der Franzosen; Italian, sifilide; Spanish, sifilis; Swedish, radezyge.

**Definition.**—Syphilis is an infectious disease, acquired by contagion or transmitted by inheritance, which runs a chronic course and exhibits both local and general constitutional manifestations. Its signs and symptoms are protean, but they are usually exhibited in a determinate order, on the basis of which several distinct clinical stages are recognized. The lesion produced is an infectious granuloma, similar to that seen in tuberculosis and leprosy.

**History.**—It is rather absurd to call attention, as is so often done, to the obscurity which enwraps the origin of syphilis; for it is an obscurity about which there is nothing odd and one which syphilis shares with many diseases. In a few instances—the English sweating sickness is an example—we know with exactness the whole history of a disease; but inquiries of this kind lead, as a rule, by way of increasingly inaccurate data to a labyrinth of confusion for which incomplete medical information, insufficient medical equipment, and fantastic medical hypotheses are responsible. That such is also the end of effort in the case of syphilis is, then, a pronouncement which, although made with all the seriousness of disappointed Teutonic industry, is in no way striking. It is, on the other hand, equally true that many contagious diseases have at some point in history spread at such a rate and over so great a territory that the names "pest" and "plague" have been applied to them; their phenomena have been so obvious as to be described as new; and attention has been so generally drawn to them that subsequent authors have been tempted to regard this unusual assertion of the disease as in reality its first appearance. Here, again, syphilis has shared the fate of many contagious diseases; and if one keeps in mind these two facts—the obscurity surrounding the first appearance and early manifestations of the disease, on the one hand, and its well authenticated spread at a definite point of history, on the other—he has only to fill out this skeleton with a few data in order to sketch the history completely.

There is surely no reason to imagine, *a priori*, that mankind in its infancy was free from syphilis. The positive evidence that such was not the case, afforded by the discovery of syphilitic bones of great antiquity, was discredited by Virchow; but there is scattered mention by medical and lay writers, of symptoms which, although often misinterpreted at the time and never collated

as the phenomena of one clinical entity, nevertheless strongly suggest the existence of the disease in ancient times. As long ago as B.C. 2637[1] Nusi King, a Chinese writer, described the phenomena of venereal disease and among them the symptoms of lues. In India it seems probable that syphilis existed centuries ago; and in the Hebrew Scriptures one meets many references, some of which may, others of which undoubtedly do, contemplate venereal disease. There are, for example, the "emerods in the secret parts," the "botch of Egypt," the "scab," the "itch whereof thou canst not be healed;"and the unclean man with a "running issue out of his flesh." One finds ground, therefore, for feeling certain that antiquity was to a degree, at least, syphilized. And if it was syphilized at all it seems likely, from the well-authenticated license of the times, that the disease was fairly rampant. We know what *could* happen on occasion, as when the daughters of Moab vexed the Israelites with their wiles, and Zimri and Bozbi, the Midianitish woman, perished together; "and those that died in the plague were twenty and four thousand." Nor is it anything less than history that in various countries cults were flourishing which, under the cloak of religion, were lending to the most lascivious of orgies the dignity of worship. There was the Lingam and Phallus cult; there was the Baal and Astarte worship in Assyria and elsewhere; there was the Aphrodite and Dionysus sect in Asia Minor; there was the Venus and Bacchus and Priapus worship in Rome. Here were religions not merely tolerating and countenancing sexual excess, but incorporating in their liturgies the wildest license and eliminating not only chastity, but even continence, from their rubrics. Surely syphilis found in this state of affairs at least no obstacle to its advance.

And yet there seem to be good grounds for supposing that syphilis was, on the one hand, less easily acquired in antiquity than at the present time, and that its symptoms, on the other, were different in character and less serious in degree. The prevalence of circumcision, the observance of depilation, the use of baths and other cleansing processes after intercourse, and, in certain countries, the strict protection of the women, these were some of the things which checked contagion; while the universal belief, in ancient times, that the initial lesion was a serious affair, probably led to an early and heroic intervention that prevented the tragic sequelæ of a placid faith in the triviality of the early signs.

In the centuries between remote antiquity and mediæval times, venereal diseases flourished and were subjected to gradually improving medical observation. Hippocrates (B.C. 459–377) wrote (De ulceribus) of ulcers of the foreskin; Celsus (B.C. 25 to A.D. 45) mentions sores of the foreskin, glans, etc., and notices the association of buboes with them; and in the writings of Oribasius (A.D. 326–403), Aetius (about A.D. 550) and Paulus Aeginata (about A.D. 650) there are pretty clear references to venereal diseases. In Asia syphilis seems to have been in these times less frequent and less severe than in the West; and there is scanty reference to it in the writings of the Arabists. In Europe, on the other hand, syphilography began to take on dimensions with the advent of the fourteenth century. This was due in part to the immorality following the black death, in part to the influence of Arabist theories that chastity was harmful, in part to the spread of the disease by the crusades, but chiefly to the improvement in medical observa-

[1] The date is not beyond dispute.

tion. The conditions of life in the dark ages were surely favorable to the spread of venereal contagion. Since the time of Charles the Great no large city in France had been without its brothels; and the streets of Paris, observes an early writer, swarmed with prostitutes at night as they had swarmed with dogs in the day. It was not infrequent for one and the same house to contain a school on the first and a brothel on the second floor; and as early as 1163 municipal laws had been drawn up against women afflicted with "the perilous infirmity of Burning." Add to these circumstances the prevalence of war, with its invasions on one part of the world by notoriously loose characters from another, keep in mind the opportunity for transmission afforded by the crusades, and it becomes plain that existent venereal disease could not long remain a local pestilence.

But it was not until the end of the fifteenth century that syphilis became pandemic; and when it did so it broke loose with such violence and over such a large area that its spread took rank as one of the notable events in medical annals. The source of this great pandemic and the circumstances which made it possible have long been debated more or less fruitlessly. This much is established. Toward the end of the fifteenth century Europe experienced excessive heat, heavy rains, amounting in many districts to floods, and a famine from failure of the crops. Disease of one sort or another became rampant. There were epidemics of ergotismus, of various "pests," of bubonic plague, and of influenza (?). Petechial typhus appeared in the South and the sweating sickness in England. Last of all, Saturn and Jupiter were in conjunction (1484).[1] In 1494 the army of Charles VIII, 32,000 strong, was setting out on its wild scheme of aggrandizement with the conquest of the Italian peninsula in contemplation and a highly pious ambition to reach Jerusalem. The soldiers were French; and the French soldiers were luetic. They invaded France, and pushed their way to Naples. Charles established himself on the throne, and his army syphilized the city. Before long the whole European prairie was aflame. The Portuguese got the disease from Spain; the Poles from Germany; Russia from Poland; while France spread it to the Orient and Turkey passed it on to Persia. Nor was it a "mild syphilis" which was thus transmitted. Malignant types that are now curiosities were then the regular form of the disease and the mortality was enormous. "Many patients were completely covered from the head to the knees with a dreadful, foul, black eruption which, with the exception of the eyes, left no portion of the face, neck, chest, or pubic region free. They presented such a repulsive and pitiable aspect that, deserted by their friends and left in the open air a prey to every need, they longed for nothing but death. Others in whom the disease caused scabs, harder than the bark of trees, on the scalp, the brow, the neck, the back of the head, the chest, the back and other parts of the body, tried, by scratching, to free themselves from their severe pains. Still others were so covered with papules and pustules that it was impossible to determine their number. The face, the ears, and the nose of most of the patients were the site of thick, scabby pustules which were elevated like little rods or small horns or teeth and discharged a pestiferous ichor" (Grünpeck). Phagedenic ulcers destroyed the genitalia, the lips, the chin, the region of the eyes and the bones. The ulceration even involved the œsophagus and many perished from starva-

[1] An important causal factor, according to the poem of Ulsenius.

tion.[1] And the disease continued to spread over Europe until Astruc said that, from the Pope of Rome on his throne to the lowest scullion in Christendom, all were infected with syphilis.

The facts of the early life of the syphilitic pandemic are not known with an exactness sufficient to permit of anything better than hypothesis as to its source; but several ingenious theories have been advanced. The date of the return of Columbus' crew from their voyage to the Haytian Indians fell within a short span of the early years of the pandemic; and this coincidence was too tempting to be overlooked by investigators. On it the theory of the American origin of the European pandemic has been built; but, in spite of enthusiastic support, the theory has not withstood critical investigation. Certain students of the subject, particularly in England, have maintained that Continental syphilis was an evolution form of yaws, introduced from the west coast of Africa. Others still have regarded certain fugitive Jews and Moors, driven from Spain by Ferdinand and allowed to settle in Genoa, where they became notorious for their high mortality, as the sparks that caused the conflagration.

Syphilis has been the subject of two historical disputes: the first as to its identity with gonorrhœa, and the second as to its identity with chancroid. Among the ancients, venereal diseases were spoken of in a rather comprehensive way and clinical entities were not sharply separated. As long ago, however, as Rhazes (850–923) hard and soft sores were described and their differences in etiology recognized; and in the fourteenth and fifteenth centuries the distinction between lues and gonorrhœa was quite sharply drawn. During the European pandemic, however, when all three diseases probably flourished luxuriantly, things became hopelessly mixed; and then for over three hundred years the theory of the unity of the virus, the foundation of which seems to have been laid by Vella (1506) in his writings on the *phlegmon naturale* of Avicenna, held sway. It was developed by Astruc into the theory that, the virus being the same, the difference in the character of the lesion depended on whether a non-secreting or a secreting surface were affected; and this idea was elaborated by John Hunter, who probably did as much as anyone to retard the progress of the truth by his curious and notoriously unfortunate self-inoculations.[2] Bell, by inoculating the urethra with syphilis and producing a chancre on a secreting surface, laid the experimental basis for complete disproof of the Hunterian theory; but it continued to flourish, until Ricord, in 1838, on the basis of extensive inoculations (really made by Mairion in Louvain[3]) confirmed the conclusions of Balfour (1767) and Bell (1793). Ricord, although convinced of the dis-

[1] Was it a memory of the pandemic, possibly strengthened by things he himself had actually seen, which led Shakespeare to write (the first quarto of Hamlet belongs to 1601): "*Hamlet:* How long will a man lie i' the earth ere he rot? *First Clown:* I'faith if a' be not rotten before a' die—as we have many pocky corses now-a-days that will scarce hold the laying in—a' will last you some eight year or nine year; a tanner will last you nine year."

[2] The glans and prepuce were inoculated with gonorrhœal pus. Sores resulted, followed by buboes, tonsillar lesions, and copper-colored blotches on the skin. The experiment lasted three years and proved, writes Hunter, "first, that the matter from a gonorrhœa will produce chancres." (Hunter, *Of the Lues Venerea*, vol. ii, in J. F. Palmer's edition of his works.)

[3] Ricord, of course, made many inoculation experiments; but, curiously enough, he published no nosological conclusions from his own work.

tinction between gonorrhœa and lues, believed the secondary syphilitic lesions to be non-contagious, and the chancre and chancroid to be both luetic. It was really his scholars, Bassereau, Clerc and Fournier, who settled the question. Bassereau, in 1852, by the method of clinical confrontation, arrived at the dualistic theory as it is held to-day; in 1852, Laroyenne developed it scientifically; and in 1860, Ricord, abandoning his previous position, brought to the new view the support of his great name and authority.

The names of syphilis have been legion. During its travels about the continent of Europe the unwelcome waif, as if to emphasize its foreign origin and lay at some other door its paternity, was usually dubbed according to the country from which it came. Thus one reads of morbus neapolitanus, el mal de los Castellanos, morbus gallicus,[1] morbus burdigalensis, etc. The protective saints, too, of those afflicted with the ailment have been immortalized in the nomenclature (morbus S. Maeiri, S. Fiacrii, etc.). The name in present use dates from the celebrated poem of Fracastorius (1530), who said that the disease was first sent into the world as a punishment for blasphemy on a certain shepherd named Syphilus for his presumption in blaming the gods for a blight which had afflicted his flocks.[2] The word "chancre" is an old one and occurs in a poem of Villon.

The therapy of syphilis has passed through all the vagaries. In the pre-mercurial days great attention was paid to prophylaxis and to general hygienic measures. These were supplemented in the middle ages by invocations to the saints, pilgrimages, and the fantastic recipes of empirics; but by analogy with the treatment of other dermatoses, inunctions were soon tried for the skin lesions, and mercury recommended by the Galenists on account of its "coldness" took the first place in the therapy. Since then the luetic cloud has had a quicksilver lining. Mercury was also used internally as early as 1525 by Benedictus, who died in that year. In the sixteenth century guaiacum was highly extolled by Ulrich von Hutten and Fracastorius; and it soon took a prominent place as a therapeutic measure. Vegetable depuratives, sudorifics, and purgatives were also extensively tried. At the beginning of the nineteenth century treatment without mercury came into some vogue under the influence of Broussais. In 1836 iodide of potassium was applied by Wallace to the treatment of syphilis in general and by Ricord to the treatment of the tertiary manifestations. "After this followed the strange extravagance of syphilization, which for a time stupefied the scientific world."

**Etiology.—Historical.**—The story of the search for the cause of syphilis is a tale to make the judicious grieve. "One hundred and twenty-five causes of syphilis," said Lassar, speaking in 1905, "have been established during the last twenty-five years."

The idea of a living contagium as the cause of syphilis is of course an old one; but the story of its "discovery" began in the seventeenth century with the finding, by Kircher (1658) and Abercromby, of a contagium animatum (vermiculi). Seventy years later Deidier was describing "vers vénériens" as responsible for the venereal virus. In 1837, Donné, using better microscopes than his predecessors, found the *Vibrio lineola* in the pus from

[1] That this is be translated "French disease" is not beyond dispute.

[2] The etymology of the word is uncertain: σῦς, sow, and φιλέω, I love; and σιφλός, crippled or maimed, have been suggested.

chancres, buboes, and balanitis; but he regarded its presence there as accidental.[1]

In 1869 the first cause of syphilis was "established." In this year Hallier found in the blood and pus of syphilitics the *Coniothecum syphiliticum*. Klotsch was soon in the field with an organism, and was shortly followed by Brunekens. Then came Salisbury with his *Krypta syphilitica*, and Lorstorfer with peculiar bodies which he had unearthed; and, in 1879, Klebs with his *Helicomonaden*. A little later Martineau and Hamonic "produced syphilis" in a pig by inoculating it with certain bacterial and micrococcal forms which they had isolated; the successful attack of Koch, however, proved their labor vain.

But in 1884 it did look as though the problem were to be solved. In that year Lustgarten described a characteristic bacillus found in both the primary sore and the internal organs. The organism was present in all of the 16 cases examined. Its morphological characteristics were, in a general way, those, as we now know, of the tubercle bacillus; and the bacterium was similar in its indifference to aniline dyes, although much less strongly acid-fast than Koch's organism. It was found only in peculiarly and elaborately stained specimens, was never cultivated nor successfully inoculated, and the observations of subsequent investigators, along the lines advanced by Lustgarten, gave contradictory results. The next year, however, Alvarez and Tavel, working in Cornil's laboratory, described the smegma bacillus; and the similarity of some of its varieties[2] with the organism of Lustgarten could not but be noticed and be thought of as accounting for the observations of this author. It cannot, indeed, be said that the subject was then, or subsequently, entirely cleared up; many observers maintained that the smegma bacillus was easily distinguishable from the Lustgarten bacillus and that the readiness with which the latter gave up its stain to strong acids made confusion with Koch's organism impossible, but the Lustgarten bacillus remains to this day somewhat of a bacterial mystery. The highly probable hypothesis is that the organism seen in the internal organs was, as Baumgarten suggested, the tubercle bacillus, and that the presence of the smegma bacillus about the genitalia accounted for Lustgarten's findings in chancres.

But the story did not end here. Endless "discoveries" were made, only the more important of which can be mentioned. Disse and Taguchi were soon announcing the discovery of bacilli in syphilitic blood; Neusser and Gollasch (1894) were finding a cladothrix, and Doehle, flagellated bodies; Van Niessen was describing a pleomorphous bacillus (*Bacillus veneris*), found in the tissues and the blood, and obtained in pure culture from a number of cases. Kremer (1896) was writing of the syphilis aspergillus and Tarnowsky of mixed infections; Paulsen (1901) was describing acid-fast bacilli in syphilitic blood, while Joseph and Piorkowski were claiming as specific an organism obtained from luetic sperm. Then came the announcement by Siegel of his observation of the *Cytorrhyctes luis*, an organism found not only in smears from luetic lesions, but also in the tissues and the blood

[1] Rille has recently shown that the organism observed by Donné was in all probability the *Spirochæte refringens*.

[2] The smegma bacillus is commonly spoken of, in connection with its similarity to Koch's organism, as though it had an unvarying morphology. As a matter of fact, its shape ranges all the way from that of a coccus to that of a streptothrix, and it is only certain forms which may be confused with the tubercle bacillus.

of rabbits and apes inoculated. The finding did not receive corroboration from other observers; it could not be substantiated by Neisser in experimental work on apes. But it must not be forgotten that the work of Siegel gave a new impulse to the study of the cause of syphilis and that it was the investigation of his findings which led Schaudinn to his own discovery.

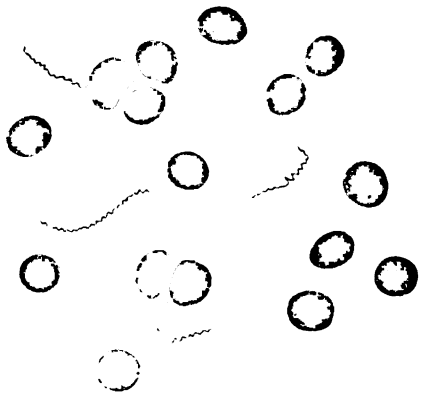
**The Spirochæte Pallida.**—It was in 1905 that what seems like the final word on this subject was spoken by two German investigators.[1] On May 17th of that year the paper of Schaudinn and Hoffmann was read before the Berlin Medical Society. They had already made a preliminary report of their findings, but their Berlin paper was accompanied by microscopic demonstrations. It was a model of calmness; and despite the conviction which they must have had that they had got "to the quick of the ulcer," they presented the facts quite simply and left etiological deductions to others. They had found, they said, a characteristic organism in syphilitic lesions; it was readily told from other similar bacterial forms and had been present in the primary sore of 7 cases examined; in the anal papules of 1 case, in the genital papules of 8, in 2 closed primary lesions of the skin of the penis, in inguinal buboes in 12 cases, and once in the splenic blood. Control examinations of soft chancres, of carcinomatous, sarcomatous, and lupous tissue, and of the glans of balanitis failed to reveal the organism. Moreover, Metchnikoff had examined the primary lesion in experimentally inoculated apes, taking his specimens shortly after the appearance of the sore and before ulceration, and had found the spirochæte of the authors.

In 1903, Borrel and Gonjou had found an organism in smears from hard chancres and from mucous lesions of the throat, which appears now to have been identical with the spirochæte of Schaudinn and Hoffmann; Bordet had also made similar observations in Brussels; but these authors either did not appreciate the significance of their observations or were unable to impress its significance on others; and it was not until the appearance of the work of Schaudinn and Hoffmann that the scientific world again set seriously to work on the subject. Almost immediately corroboratory reports were coming in. By December, 1905, the *Spirochæte pallida* had been found by various observers all over the world in the following syphilitic lesions: smears from and sections of primary genital and extragenital sores, both ulcerating and intact; eroded and intact papules of the penis, anal region, and skin in various parts of the body; psoriasis palmaris; pustules; mucous patches; smears from artificial vesicles over and sections of the roseolar rash; rupia; primary and secondary lymph glands in various regions; blood, both circulating and splenic; tertiary cutaneous syphilides; gummata, both closed and open, and in the cerebrospinal fluid. In congenital cases the organism had been seen in pemphigus, in papules, in artificial vesicles over the normal skin, in secretions of the mouth and nose, in the blood, in smears from and sections of thymus, lungs, liver, spleen, kidneys, adrenals, lymph glands; in the bone-marrow, the meninges, the cerebrospinal fluid, and the placenta. Furthermore, the examination of primary sores in the experimental syphilis of

[1] The enormous literature on the *Spirochæte pallida* is well reviewed up to December, 1905, by Julius Glass in a Leipzig thesis (Ueber Spirochæte pallida). The complete literature is also given by Herxheimer in Lubarsch and Ostertag's *Ergebnisse der allgemeinen Pathologie*, Jahrgang xi, ab. 1. The early articles of Schaudinn and Hoffmann appeared in the *Arbeiten aus dem Kaiserl. Gesundheitsamt*, Bd. xxii, H. 2, S. 527, and in the *Deutsche med. Wochenschr.*, 1905, Nr. 18., S. 711.

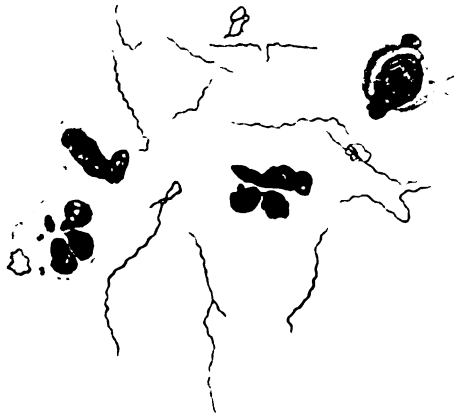
# PLATE I

FIG. 1



Spirochæte Pallida. Smear from Hard Chancre.
Giemsa's stain. × 1000.

FIG 2



Spirochæte Refringens. Smear from Chancroid. × 1000.

monkeys, made by numerous competent observers, showed the presence of the *Spirochæte pallida*. On the other hand, reports of control examinations of non-luetic lesions were strikingly unanimous in asserting the absence of the organism. The vast amount of work done in the last two years has tended only to confirm these early findings both as to the presence of the *Spirochæte pallida* in luetic lesions and as to its absence elsewhere.

There have been, it is true, publications on the other side of the question. Kiolomenoglou and v. Cube claim to have found in balanitis and other non-luetic conditions a spirochæte which could only be identified with the pallida, and their claim was supported by a small number of authors. Hoffmann and Schaudinn saw their specimens, and decided that the organism observed was not the *Spirochæte pallida*. Saling, too, struck by the frequency with which smears made from the organs of congenital syphilitic cases were negative, while stained sections of the same organs showed the spirochætæ in great numbers (a phenomenon, he asserted, true of no other organism), contended and still maintains that the structures seen in stained specimens are nothing more than tissue fibrillæ, and that their presence is explained by the preceding inflammatory and degenerative processes which the disease has caused. His views have not met with much support; and a case recently seen at the Johns Hopkins Hospital suggests that the presence of the *Spirochæte pallida* in the organs of cases of congenital lues can be accounted for in no such way. A syphilitic woman presented herself to the out-patient department of the obstetrical service about the sixth month of pregnancy. She was at once put on mixed specific treatment and carried her child until the ninth month, when she was delivered. The child was alive, but died within twelve hours. The placenta was luetic and pathological examination of the organs of the child showed all the lesions of syphilis; yet continued and careful search of smears from and sections of the organs failed to reveal a single organism. The inflammatory and degenerative changes of Saling were certainly present, but the "tissue fibrillæ" were absent. Whether the spirochætæ had been actually killed off by treatment, or had been absent from the first, it is of course impossible to say, but the case offers the strongest evidence against the views of Saling.

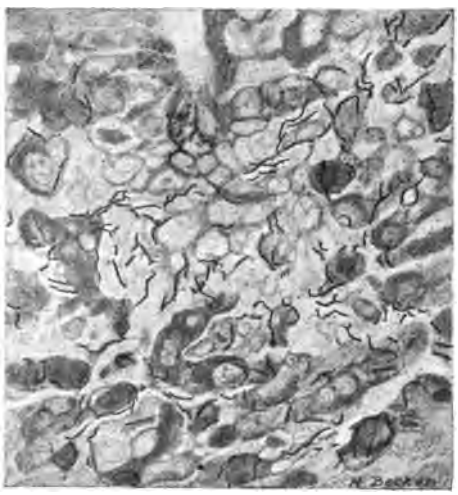
The *Spirochæte pallida* (Plate I, Fig. 1) is a long, delicate, non-refractile, spirally curved organism. It was first studied with very high magnifications (1200 to 2800), but it may be seen quite well with the ordinary oil-immersion lens. Its average length is from 4 to 14 $\mu$; smaller forms, 2 to 3 $\mu$ in length, are, however, also seen, and organisms 20 $\mu$ long have been observed. It is pointed at both ends. Its spirals are sharp, clear-cut, tight and corkscrew-like, and are less definite toward the ends than elsewhere. They vary in number from six to twenty-six, but shorter forms with only two or three curves are also seen. The length of each spiral measures from $\frac{1}{5}$ to $1\frac{1}{2}$ $\mu$, and the large number of spirals in proportion to the length of the organism is a characteristic feature. The whole organism is usually somewhat curved; it may be S- or C-shaped and occasionally forms a closed circle.[1] It is circular in cross-section. In both stained and fresh specimens flagellæ have been seen, usually one at either end, although occasionally more. The flagellæ are extremely delicate and are about as long as four to six spirals of the organism. The motility

[1] This picture is probably caused by two C-shaped organisms in apposition.

of the *Spirochæte pallida* is of three kinds: rotation on the long axis, snaky, whip-like undulations of the whole body without locomotion, and forward and backward movements. The motion persists, if physiological salt solution be added, for six hours; it is stopped by glycerin, and gradually disappears on exposure to the air. Certain observers, however, have been able to see in the organism nothing more than Brownian movements. Unlike other spirilla the *Spirochæte pallida* retains its spiral form when at rest. The presence of a surrounding undulating membrane seems probable; Schaudinn claims to have observed it best in specimens stained by the Loeffler method for flagellæ.

When examined with an ultra-microscope, bodies suggestive of nuclei have been seen, but the presence of a nucleus is not beyond doubt. The organism probably multiplies, like the trypanosomes, by longitudinal fission; no signs of transverse division have been observed. It does not bear spores. In smear specimens the *Spirochæte pallida* usually lies free and is seldom enclosed in a cell. It is, however, frequently in intimate relation with a red blood cell, often touching it with one end and not infrequently embracing it. The organisms may lie separate from one another; but often they lie in groups (agglutination of Levaditi, accolement des spirochètes of Favre and André), and occasionally they form definite tangles. Their life history is not known; what have been described as involution forms are occasionally seen. Schaudinn regarded certain of the oval and spindle-shaped forms as resting stages. One of the marked characteristics of the organism is its tinctorial obstinacy. No stain colors it deeply and many do not color it at all. It does not stain by Gram's method. In sections of chancres the *Spirochæte pallida* lies in the epithelial layers of the epidermis, in the lymph spaces, and in the thickened vessel walls. According to Levaditi it is first seen free within the vessels; thence it passes to the endothelium, where it causes the swelling and occlusion characteristic of the pathological picture of the disease. It is seen in greatest number in sections of organs from children dead of congenital syphilis; in these cases the tissues may literally swarm with the organism (Fig. 19). Most authors hold that the *Spirochæte pallida* is transmitted by the blood stream. Its modification and final disappearance from a lesion during specific treatment have been frequently observed; but similar observations have been made during the spontaneous healing of chancres, and it is not definitely established that the treatment (whether local or general) is responsible for the disappearance of the organism.

FIG. 19



Section of lung, congenital syphilis. × 800.

*Method of Obtaining the Organism.*—To examine a chancre for the *Spirochæte pallida* the surface should first be well cleansed with soap and water, rinsed, and dried. It is important that this be done with care, for thorough cleansing removes large numbers of the *Spirochæte refringens*, the organism usually present on the surface of sores, and, from its similarity with the *S. pallida*, offering difficulties in the microscopic diagnosis. The lesion should then be lightly curetted and the slight oozing checked by pressure with a piece of gauze. After any blood still present has been wiped away, the sore is then squeezed between the fingers until a drop of blood-tinged serum exudes. This is used for the examination, either a hanging drop or a thin smear preparation being made from it. If the chancre be covered with epithelium one can either remove the covering mechanically or obtain a drop of serum by aspiration. Enlarged lymph glands may be easily examined by withdrawing a drop of serum from them with an ordinary small aspirating syringe. Serum for smears may be obtained from lesions of the exanthemata by scraping off the covering epidermis. Certain observers have recommended the formation of artificial blisters by vesicants and examination of the serum obtained from them by aspiration. For examination of the blood the method of Noeggerath and Staehelin is best: 1 cc. of blood is removed and mixed with 10 cc. of $\frac{1}{3}$ per cent. acetic acid. The mixture is then centrifugalized and thin smears are made from the sediment.

*Staining the Organism.*—It is of first importance that the staining and examination be promptly done; for the organism stains badly, and sometimes not at all, in smears that are not perfectly fresh, and the color after staining gradually fades. The smear may be well fixed by simple air drying. Fixation by the vapor of osmic acid is said to give good definition and to bring out the tapering extremities particularly well; this may be readily accomplished by placing the specimens for a few seconds over the mouth of a bottle containing osmic-acid crystals.

Staining methods for the *Spirochæte pallida* are almost as numerous as the investigators who have studied it. On the whole, the modification of Giemsa's method, recommended from the first by Schaudinn and Hoffmann, is probably the best, although it is time consuming. According to the technique originally advised, the specimen is placed, after fixation, in freshly prepared Giemsa's azur-eosin[1] and allowed to stay twenty-four hours. It is then washed with water and examined. At present, a slight modification of this method is widely used. The Giemsa stain now used is known as "Giemsa-Lösung für die Romanowsky-Färbung," may be obtained from Grübler in Leipzig, and has the following formula:

| | |
|---|---|
| Azur II-eosin | 3.0 gm. |
| Azur II | 0.8 gm. |
| Glycerin (Merck, c. p.) | 250.0 gm. |
| Methyl alcohol (Kahlbaum I) | 250.0 gm. |

The specimen is dried in the air and hardened in absolute alcohol for one hour. The stain is then diluted with distilled water (1 drop of stain to 1 cc. of water), a fresh dilution being made for each examination. In this diluted

[1] Following is the formula:

| | |
|---|---|
| Giemsa's eosin (2.5 cc. 1 per cent. eosin to 500 cc. water) | 12 parts |
| Azur I (1 to 1000 water solution) | 3 parts |
| Azur II (0.8 to 1000 water solution) | 3 parts |

stain the specimen is allowed to remain for twenty-four hours. Good results may be obtained if the stain stay on for only half an hour, but they are not quite so certain. In this stain the *Spirochæte pallida* is colored a delicate violet purple. The nuclei of the leukocytes should be colored a deep blackish red; if this is not the case the specimen has not been properly stained. Probably not all the organisms take up the stain; for they are not as numerous in a stained specimen as in a hanging drop from the same source.

Many other staining methods have given good results, particularly various other modifications of the Romanowsky stain. A very easy method is simple heating for two or three minutes in Victoria blue. MacNeal has also recommended a method which is quick, simple, and satisfactory. The specimen is heated on a cover-glass for forty-five seconds in the following solution:

| | |
|---|---|
| Methylene violet (crude) | .25 |
| Methylene blue (medically pure) | .10 |
| Eosin (yellowish) | .20 |
| Methyl alcohol (pure) | 100.00 |

It is then dipped in a 1 to 20,000 sodium carbonate solution, moved about in it for one to two minutes, washed with water, and examined. The spirochæte is stained a delicate blue, or nearly black if the staining be prolonged.

For demonstrating the organism in sections the best method is that of Levaditi; it is a modification of the technique of Ramon y Cajal used for nerve fibers. Small pieces of the tissue, about 2 mm. thick, are hardened in 10 per cent. formalin for twenty-four hours. They are then left for the same length of time in 25 per cent. alcohol. After washing with water they are placed in a freshly made 1.5 per cent. watery solution of silver nitrate and left there for three days at blood temperature and protected from light, the solution being changed each day. They are then put into the following solution and left for twenty-four hours at room temperature (light excluded).

| | |
|---|---|
| Pyrogallic acid | 2.0 gm. |
| Formalin | 5.0 cc. |
| Distilled water | 100.0 cc. |

After washing with water they are dehydrated with 85 per cent., 95 per cent., and absolute alcohol, and then enbedded. For demonstrating the flagellæ, very thin smears are necessary. Schaudinn recommends that the specimen be heated to boiling in the following solution:

| | |
|---|---|
| Tannin 25 per cent. | 10.0 |
| Cold-saturated solution ferrous sulphate | 5.0 |
| Saturated alcoholic solution of fuchsin | 1.0 |

Counterstain with Ziehl's fuchsin.

*Diagnosis.*—The *Spirochæte pallida* is probably but one member of a large group of organisms with similar morphology, and it offers therefore some difficulties in microscopic identification. The chief trouble is caused by the *Spirochæte refringens*, for this is found just where the pallida is likely to be sought for. It occurs, for example, in the mouth, on the tonsils, in ulcerating lesions, in smegma, and on venereal warts. The *Spirochæte pallida* can, however, usually be recognized by its delicacy, its slight refractility, its tinctorial obstinacy, and by the number and tight, corkscrew configuration of its spirals. The refringens (Plate I, Fig. 2), on the other hand, is larger,

thicker, more refractile, and quite easily and deeply stained; but most characteristic of all are its spirals, which are broad and wavy or undulating, rather than corkscrew shaped. Its ends are rarely pointed and often blunt, its movements are more rapid than those of the *Spirochæte pallida*, and it occurs in great numbers in smear specimens. Not more than 2 or 3 of Schaudinn's spirochætæ, on the other hand, are usually seen in one field of a smear from a chancre; and often they are much less numerous.

*Classification.*—There is still dispute as to the classification of the *Spirochæte pallida*. Schaudinn regarded it as a protozoan, distinguished from the other spirochætæ, on the one hand, by its preformed spiral morphology and by its possession of flagellæ, and from the spirillæ, on the other hand, by the flexibility of its spirals, by the possession of only one flagellum at either end and by its apparent capacity for longitudinal fission. He agreed with Vuillemin's suggestion that the organism be called a Spironema.

*Significance.*—To attempt to speak positively about the specificity of this organism is to render a verdict on evidence which is not absolutely complete; and the unfortunate history of syphilis in this regard is a warning against premature judgment. A consideration of the present status of the question should contemplate the following facts:

1. Experts are almost unanimous in regarding the specificity of this organism as a "probability bordering on certainty." No one regards its specificity as proven, and there is everywhere an admirable caution evident in regard to opinions about the causal relation of the organism to syphilis; but it is most striking that the very extensive and careful scrutiny to which the *Spirochæte pallida* has been subjected, although it has brought out confirmatory observations in great number, has failed to reveal a single well-established fact at variance with the idea that this organism is really the cause of lues.

2. The *Spirochæte pallida* occurs almost constantly in primary and secondary luetic lesions. Failures to find it date largely from the early period of the search for it, before the technique was developed or the eyes trained; and the growing experience of clinics throughout the world is that the organism of Schaudinn and Hoffmann will be found in chancres if carefully and persistently looked for.

3. The *Spirochæte pallida* occurs unmixed with other organisms in the depths of primary and secondary luetic lesions, and in the blood.

4. It is in the most contagious syphilitic lesions (the chancre, the condyloma, and the mucous patch) that the *Spirochæte pallida* is most often found and in greatest number.

5. The *Spirochæte pallida* occurs in the internal organs, the specific exanthemata, and in the blood of congenitally syphilitic children. It is also found in the placenta and in the umbilical cord, and the absence of other organisms in these situations is a striking fact.

6. The *Spirochæte pallida* is absent from non-luetic lesions.

7. The *Spirochæte pallida* disappears, in some cases at least, under the treatment which cures the syphilis. In at least one congenital case it was entirely absent from the organs of a definitely syphilitic child, whose mother had received specific treatment for some weeks before delivery.

8. The *Spirochæte pallida* is less numerous in healing sores than in others.

9. The *Spirochæte pallida* does not pass through a Ton-filter. This fact is rendered striking by the observation of Metchnikoff and Klingmüller that the syphilitic virus behaves similarly.

10. The *Spirochæte pallida* has been a frequent, although not an absolutely constant, finding in the experimental syphilis of apes, not only after inoculation from human cases, but also in the disease transmitted from one animal to another. Its absence from the normal skin of the ape has been established by Kraus. Neisser's failure to find it in the internal organs and blood of experimentally syphilized monkeys and in the hereditary syphilis of monkeys remains unexplained.

11. Cultivation of the *Spirochæte pallida*, and therefore, obviously, experimental production of syphilis by inoculation of the pure organism, remain impossible. Koch's third and fourth laws are, therefore, still unsatisfied; but the third law is also unsatisfied in the case of the malarial plasmodium, the etiological nature of which no one doubts.

The value of the *Spirochæte pallida* from a diagnostic standpoint seems, at least, to be established. Whether we regard it as the causal agent or as a saprophyte, its almost constant presence in chancres and absence in non-luetic lesions is almost beyond dispute; and we are therefore justified, in the event of a positive microscopic finding, in making a positive diagnosis of syphilis and in instituting treatment on this evidence alone. If a single examination, however, be negative we are not justified in regarding the lesion as non-luetic, just as we would be without justification in regarding a sputum as non-tuberculous after examining one smear preparation. Recourse must be had to repeated examinations; if these continue negative, we can say, with the very highest confidence, that the sore is not luetic.

**General Pathology.**—Syphilis, which begins its pathological existence as a modest, inactive Hunterian chancre, soon enters upon a career that is unsurpassed for the inclusiveness and variety of its manifestations. There is no organ in the body,[1] nor any tissue in the organs, which syphilis does not invade: and it is therefore manifestly difficult to speak, at least at all concisely, of the pathology of the disease; just as it is almost impossible to describe its clinical symptoms without mentioning almost every symptom of every disease known. Certain general pathological features are, however, characteristic, and these must be here described; the other more specific changes will be treated under affections of special organs. One notices throughout the pathological changes of lues the cellular infiltration and the prominent part taken by the bloodvessels, both of which features have been seen to play such an important role in the chancre. Virchow, indeed, called attention to the fact that all the syphilitic lesions from the chancre to the gumma are granulomata so much alike that they cannot be differentiated.

1. **The Syphiloma.**—The following are the features of the general pathological anatomy of the syphiloma as outlined by Jullien:

"(*a*) Infiltration of the derma and the mucous layers with small cells. These cells, which closely resemble the aspect of embryonic elements encountered in fleshy granulations, are heaped up at the periphery of the vessels, between the trabeculæ of the corium, and finally involve the papillæ and Malpighian bodies to such a degree that the limitation between these two layers of the skin entirely disappears.

"(*b*) The inevitable destruction of those cells which are incapable of organization. At the end of a certain time the infiltrate undergoes a fatty degeneration and enters into the organism by resorption or ends in a purulent dissolu-

[1] The prostate is a possible exception.

tion. In any case the vitality of the secondary syphiloma is not sufficient to transform it into definite tissue. After its disappearance the elements of the tissues in the midst of which it was established again take on their normal disposition without any necessary loss of substance.

"(*c*) The centrifugal course of the neoplasm, both in its development and in its retrogression. It is always from the centre to the periphery that the infiltration takes place; the borders of the lesion are consequently more recent than the centre; hence the differences in aspect which may be presented in the two parts. When the centre becomes depressed under the influence of retrogression, the neoplasm may maintain its maximum of development at the borders; this is the reason for certain forms (cup-shaped, annular, etc.)."

The pathological changes explain the features of the various lesions. "The papule," for example, "is prominent because there is cellular infiltration; hard, because this infiltration is dense; it is brilliant, because the epidermis is tense over the summit; surrounded by a collarette, because the coloring matter of the blood furnishes an extravasation; and, finally, when resorption takes place, the epidermis wrinkles at its surface and is eliminated by an ephemeral desquamation."

2. **The Cutaneous Syphilides.**—These cannot be treated in detail on account of their multitudinous varieties. The pathology, however, of the macule, the papule, and the pustule will suffice as examples of the characteristic changes. The *macule* consists of an exudation of leukocytes and plasma cells about the small vessels, a proliferation of connective tissue, an infiltration of the hair, sweat and sebaceous follicles, with round and plasma cells. Horny pigment cells are occasionally deposited in the papillæ (Ehrmann's melanoblasts). The *papule* represents a further development of the macule, due to an advance in cell proliferation toward the surface and toward the depth. Plasma cells and leukocytes occur in groups ("Zellenwucherungen"), often about the ducts of sweat glands. Round cells are numerous and giant cells frequent. Exudation of leukocytes and transudation of serum into the epidermis may occur and the papule may, therefore, be accompanied by a pustule or vesicle. The *pustule* presents a similar picture except that suppuration is now present at the mouth of hair follicles or sebaceous glands. The walls of vessels, hair follicles, sebaceous and sweat glands show cellular proliferation and infiltration of cells, which reaches to the horny layer, obliterating the distinction between rete and cutis. Giant cells are present.

3. **The Gumma.**—This lesion belongs to the infectious granulomata and shows no specific elements or structure. The pathological changes are similar to those of the papule, but destructive changes are present and give the lesion its character. There is softening of the connective tissue, which is transformed into a thready, mucoid mass, consisting of detritus and cells which have undergone fatty degeneration. Lymphoid, pus, and epithelioid cells are present. At first there are no new bloodvessels formed, but later these become a feature. The overlying epidermis becomes inflamed and the upper layers of the corium swollen with a semiliquid infiltration. The gumma may be surrounded by dense, sclerotic, scar tissue, and present undeniable histologieal analogies with tubercle, both of which tend to "caseation." The gumma, however, may be absorbed and finally disappear without degeneration or ulceration; this is a remarkable characteristic and is well illustrated in gumma of the testicle, where the organ may be reduced to one-

fifth its size without signs of breaking down. The gummatous change may be diffuse, rather than confined to the limits of an infectious granuloma. The microscopic distinction between gumma and tubercle is always difficult and often impossible. In general, epithelioid cells are more frequent in tubercle, fibroblasts and connective-tissue strands in gumma; in gumma, caseation and connective-tissue proliferation are simultaneous, in tubercle the latter succeeds caseation; gummatous caseation is a much slower process than tuberculous caseation; the tubercle is often free from vessels, but new-formed vessels are a prominent feature of gumma and often persist even during necrosis. Giant cells are certainly more characteristic of tubercle than of gumma. Baumgarten goes so far as to deny their occurrence in syphilis: "The presence of a single typical giant cell of Langhans tips the scale of probability in favor of tuberculosis."

When the growth of the gumma ceases the younger peripheral cells become organized into connective-tissue cells, forming an envelope for the cheesy and gummatous nucleus. This envelope shrinks, the semifluid portions are absorbed, and finally a scar (possibly calcareous) is left behind.

4. **Lesions of the Mucous Membrane.**—When the papule occurs on mucous membranes or on moist portions of the skin it presents certain other pathological characteristics, but remains essentially a papule. Cell proliferation invades the cutis, necrosis of the surface occurs, and a characteristic deposit is formed. This is removed mechanically and is again replaced; or else the papillæ proliferate and mechanical stimulation leads to great hypertrophy, immense cauliflower condylomata resulting.

5. **Inflammations.**—Syphilis may determine inflammatory changes. Arteritis and peri-arteritis have already been referred to; pharyngitis is frequent; acute nephritis is not rare; iritis and periostitis are common, and in the lungs a chronic fibroid change is sometimes seen (the fibrous interstitial pneumonia of Virchow). The non-specific inflammation of the viscera which occurs in tertiary syphilis commences as a congestion and runs a subacute or chronic course. It ends in new connective-tissue formation, cirrhosis of the organ affected, and atrophy of its parenchyme. Later the inflammation is gummatous in character.

6. **The Blood.**—The blood picture, which is never characteristic, may vary from that of chlorosis to that of pernicious anæmia. A normal count, although unusual, occurs. A severe chlorotic anæmia is the rule in the primary stage and is most marked in women. With the appearance of the rash there is further diminution in the hæmoglobin; the red blood count may remain about where it was or drop very rapidly. In tertiary and hereditary syphilis the picture may be that of primary pernicious anæmia with numerous megaloblasts; normoblasts, gigantoblasts, microcytes, and poikilocytes are also seen. Mercurial treatment causes the red cells to rise, although its *first* effect is often a drop, accompanied, in some cases, by hæmoglobinuria. Sometimes a hypercythæmia results from the treatment; but if it be continued too long or in too large doses, mercury itself may cause an anæmia. A large inunction or injection of mercury, given after the disease has ceased to be local and has invaded the lymph glands, causes an immediate drop of from 10 to 20 per cent. in hæmoglobin, which rises, in a few days, to normal or above normal. This is known as Justus' test; it may be obtained in any case of florid lues, is not present during the early primary stage, and, while not certainly pathognomonic, is valuable.

The leukocytes are normal in the primary stage, or slightly increased. If mercury be given, the percentage of polymorphonuclear neutrophiles increases. During the secondaries there is slight leukocytosis, with increased lymphocytes and eosinophiles. The severe anæmia of the tertiary stage is often accompanied by leukocytosis with high lymphocytosis, and myelocytes occur in severe cases.

7. **Amyloid Degeneration.**—Syphilis plays an important role in the etiology of amyloid degeneration; 21 per cent. of 80 cases of amyloid degeneration studied by Hoffmann in the Berlin Pathological Institute were due to syphilis. The intestines, liver, spleen, and kidneys are oftenest involved; and the condition is common in association with rectal lues to women. It is rare in the congenital form.

**The Nature of the Syphilitic Virus.**—Acquired syphilis is transmitted only by contact, either direct (venereal, buccal, mammal, corporeal) or mediate (the various contacts of domestic, social, industrial, and professional life, such as the use of common utensils, the care of children, vaccination, etc.). Hereditary transmission may be paternal, maternal (the mother actually passing on her own infection to the product of conception, or else transmitting the disease from a luetic semen without herself receiving apparent infection), or from both parents.

The virus possesses the power of remaining dormant for a long time and suddenly rousing into activity again. It circulates in the blood, and exists in the sperm, whence it may pass to posterity. The father is, indeed, most often responsible for hereditary syphilis; but he may beget a healthy child, although himself in the acute stages of the disease, and not all congenital lues is paternal in origin, for a woman with acquired syphilis is liable to bear infected children. So long as the disease is in the primary or secondary stage it is intensely contagious; in general, the virulence decreases with the duration of the illness, and at some period of its life its contagiousness ceases. Just when this occurs no one can say; there is not even agreement as to the contagiousness of the tertiary lesion,[1] but clinical evidence goes to show that on the average a well-treated case of syphilis offers no danger of direct transmission after three years have elapsed without symptoms. The danger, however, of transmission to posterity lasts much longer—how long it is impossible to say.

The virus is certainly contained in the primary and the secondary lesions, and most abundantly in those that are secreting or degenerating. Whether the normal secretions contain it is not definitely agreed. Diday, Pardova, and others, working on the tears, milk, sweat, and urine, failed to demonstrate the presence of the virus by inoculations; Fenger, however, apparently proved that the secretions possess contagious properties when inoculated in sufficient dose. The virus rapidly loses its activity outside the human body; Boeck found that when dried upon linen it soon became no longer infectious. The virus cannot apparently enter the body except through injured skin or mucosa.

The facts as to luetic immunity can perhaps be best stated in an itemized way, but one has always to bear in mind that no statement about syphilis is always and absolutely true, and that even such well-founded generaliza-

[1] The discovery of the spirochæte of Schaudinn in tertiary lesions probably settles this dispute. Neisser and others have recently proven, by experimental inoculation of apes, that the gumma is infectious.

tions as Colles' law contemplate only a majority, although in this case it is the vast majority, of clinical observations.

1. Syphilis is exclusively an affliction of the human race. Animals do not suffer from the disease,[1] and with the exception of monkeys, an exception which has only recently achieved the distinction of well-authenticated scientific substantiation, they cannot be inoculated with it.[2]

2. In human beings there is *no absolute* immunity to the disease.

3. Syphilis does, however, confer a certain degree of immunity, and its occurrence in an individual renders a second attack quite unlikely, although not impossible. On the basis of experimental work on apes Fenger and Landsteiner reached the following conclusion: The syphilitic at all stages of the disease can react with local specific appearances to the syphilitic virus and there exists only a very considerable, but not an absolute, immunity to the disease.

4. There is a certain degree of natural immunity to the disease. The occurrence of syphilis, for instance, in only one of several individuals exposed to exactly the same source of infection is a fairly frequent clinical observation difficult to explain in any other way. Certain authors are of opinion that prostitutes as a class enjoy a relative immunity to the disease; this may, however, be simply an acquired immunity.

5. Syphilis is essentially a disease acquired in youth, and, although no age is immune, the initial sore rarely occurs after the fiftieth year. Habits of life would, of course, account for this fact; whether immunity also plays a role it is impossible to say; but the proverb of Ricord should at least be kept in mind: "Let him who lusts after syphilis make use of his youth, for in old age its acquaintance cannot be first made."

6. There seems to be good ground for believing that the existence of syphilis in a community for some length of time results in a relative immunity to it, as expressed by a lessened severity of its symptoms. This observation was strikingly made after the great European pandemic; it has been repeated since, when the disease, freshly introduced into a community and taking on a virulent form, has gradually become milder; but there is no reason to suppose that this immunity will ever become absolute and that the disease will, of itself, "die out."

7. **Colles' Law.**—"One other peculiarity," wrote the Dublin surgeon, "in the history of the syphilis infantum, and one of the most singular connected with it, is this: Suppose a child shortly after birth exhibits evidence indicating intra-uterine contamination, and that the mother herself has never showed any symptom of the venereal disease, she will enjoy a perfect immunity from being infected by her own infant, which perhaps she is even suckling; while a healthy young woman employed merely to carry it about will quickly become diseased, and still more readily if she acts as wet-nurse to it." Colles was the first to propound the generalization; but the law was first formulated by Beaumès, and may be thus briefly stated: A woman who has borne a syphilitic child is immune to syphilis,

[1] The so-called syphilis of horses (Beschälenkrankheit), which affects asses as well, although clinically so similar to syphilis as to defy differentiation (Fournier and Jullien), is not generally regarded as identical with human syphilis.

[2] The inoculation experiments made upon other animals have been, at least, contradictory, and, as a rule, unsuccessful. Certain observers have claimed that the disease may be transmitted to the pig.

although she may present no signs of the disease. Whether the immunity is real, or whether the mother acquires it by being herself infected, although so lightly as to cause none of the usual symptoms, is still a moot question.

8. **Profeta's Immunity.**—When a woman suffering from syphilis in its contagious stage bears a child which shows no taint, the child may be suckled by its mother with impunity and will not contract the disease from her. This fact was first stated by Behrend, but was repeated by Profeta, whose name has since been coupled with it. It should be borne in mind that immunity of this sort is only transferred while the mother is suffering from active syphilis; the law cannot be extended to include all the offspring of a luetic mother. This immunity may be only an apparent one in the sense that the child has received a true but latent infection; this is the view Diday and others have upheld in order to explain late hereditary syphilis.

9. When syphilis is inherited it is usually the eldest child which suffers most, and often it is the firstborn only.

10. When a woman is infected with syphilis after conception, the child is apparently often immune. It may, however, be born syphilitic, and placental transmission is a well-recognized fact.

11. The question of the transmission of syphilis to the third generation is not settled beyond all dispute. Cases of pronounced congenital syphilis have been met with in the children of healthy parents; but the existence of a cured acquired syphilis in the parents can seldom be absolutely excluded. The reported cases do not bear careful scrutiny and transmission of syphilis to the third generation, if it takes place at all, is certainly not a common occurrence. Fournier is, however, strongly of the opinion that heredo-syphilis may have the same harmful effect on the fœtus as acquired syphilis; in the same way as the latter, it constitutes a predisposing cause for abortions, still-births, and the early death of infants.

**Clinical Features of Syphilis.**—Syphilis was divided by Ricord into three clinical stages, and to these others have added a fourth. The primary is the stage of the chancre; the secondary is the stage of the acute general invasion of the virus; the tertiary is the stage of the late, relatively non-virulent, localized manifestations, and the quaternary is the stage of the parasyphilitic phenomena. The division is, of course, more or less an academic one; no disease, syphilis least of all, follows any rule in its clinical phenomena. Nor is the evolution of the disease so constant or orderly an affair as the classification of Ricord might suggest. One of the stages may be entirely absent; the secondary and tertiary stages may be separated by long intervals or be almost simultaneous, and almost any variation of the scheme may be at times observed. On the average, however, it represents an approximation to the truth; and while its limitations must be constantly and clearly kept in mind, its value both in guiding clinical observation and in facilitating clinical description cannot be questioned.

**The Chancre.**—(*Synonyms:* infectious, indurated, or Hunterian chancre; initial sclerosis.) Syphilis makes its debut in the guise of the Hunterian, or hard, chancre, which appears as a rule within the first three weeks after infection, rarely earlier than the tenth day. Attention is frequently first called to the lesion, as Hunter observed, by an itching in the affected part; but the sore, both at its onset and later, is usually quite painless and free from sensitiveness on pressure. Its very early appearance varies greatly and at this time diagnosis is often quite impossible. "In the early part of

my life," wrote Colles, "I thought I could tell what was a chancre; but I am now convinced that a primary venereal ulcer may *begin* in any one possible form of an ulcer." Usually it is a small papule which is first noticed. As the sore develops, however, it takes on more or less diagnostic characteristics. It forms a brownish-red, firm, often button-like nodule with a shallow surface depression. Its size, shape, and consistency vary greatly; but characteristically it is circular or oval, measures 1 x 1.5 cm., and is quite hard. Its edges are sharply defined and the induration about it does not, as is usual in other inflammations, extend far beyond the limits of the lesion itself, but terminates abruptly. Its extreme motility is a characteristic feature. At this stage the chancre is really an exulceration resting on an indurated base. The surface of the base is regular, brilliant red (much the color of muscle), and on a level with the surrounding tissues or slightly above them. Its centre is not infrequently grayish or diphtheroid. The secretion is scanty and thin, and suppuration does not usually occur. If the lesion be on a mucous membrane, the surface remains moist and glistening; but in chancre of the skin the secretion often dries and forms crusts. It may, however, be altogether absent. The induration, which may feel like parchment, is usually more resistant and elastic, resembling cartilage. The sore is typically single, but in about one-fourth of the cases it is multiple; Fournier has reported a patient exhibiting twenty-six simultaneous initial lesions.

The chancre is usually accompanied by no general constitutional disturbances. Involvement of the neighboring lymph channels, particularly along the dorsum of the penis, is seen, but it is not associated with inflammatory redness. Soon after the appearance of the chancre the neighboring lymph glands become enlarged, forming, when the sore is a genital one, the characteristic luetic inguinal buboes, most frequently seen in both groins. They remain discrete, are hard, free from tenderness, and do not suppurate. They survive the chancre and become, later, part of the general adenopathy of the secondary stage. Enlarged inguinal glands are occasionally entirely absent.

*Complications.*—1. The chancre is sometimes accompanied by marked inflammatory reaction. This often takes the form of intense œdema and phimosis. A condition of elephantiasis may be present and gangrene is occasionally seen.

2. Not infrequently the chancre becomes phagedenic. This is most often seen in old men and in diabetic or otherwise diseased patients.

3. The Hunterian chancre may be accompanied by a soft chancre, and this mixed infection is frequently seen in large dispensaries. Very often, too, the evolution of a soft chancre into a hard one is observed. This is, of course, due to a mixed original inoculation; the soft sore, with a short incubation period, appears first, its base becomes gradually indurated and soon takes on the typical Hunterian characteristics (mixed chancre).

*Site.*—Chancres may be either genital or extragenital. About 8 of the latter are seen to 90 or 100 of the former. The characteristics of the lesion vary with its site and induration is usually less marked in chancres of the skin than of the glans, and in women than in men.

(*a*) *Genital Chancres.*—The primary lesion is usually situated on the genitals. In men it is most frequently seen, as Hunter observed, on the frænum and coronal sulcus; but the glans, the urethra (as far as the fossa navicularis), the dorsum of the penis, and the scrotum are occasionally the site of chancre. In women it may occur anywhere on the external genitalia, and even in the

cervical canal itself. Perigenital chancres are seen on the mons veneris, the inner surface of the thighs, and the perineum.

(*b*) *Extragenital Chancres.*—The contagion of syphilis, although usually spread by normal sexual intercourse, is not necessarily so transmitted; and the primary lesion is by no means always found on the genitalia. In certain regions of Russia, for example, where there are no physicians and where the most wretched hygienic conditions prevail, syphilis is, according to Tarnovsky, in 70 per cent. of the cases transmitted by extragenital contagion. In these districts there are few if any prostitutes, and "rural syphilis in Russia is first and foremost syphilis of the innocent."

Perverted intercourse for very obvious reasons may account for extragenital chancres; so, too, may certain of the contacts of every-day life (contagion from drinking cups, kissing, barbers' utensils, etc.). More frequent, however, are the extragenital sores acquired by the special contact of physicians and obstetricians and gynecologists run a particular risk in this respect. Chancres have also been transmitted by surgical instruments; the Eustachian tube has been infected by a catheter; the disease has been transferred from one patient to another on a silver-nitrate stick; vaccination and tattooing have spread it; and in the Continental countries the industry of wet-nursing is a well-recognized and somewhat dreaded source of contamination. Extragenital chancres are, therefore, often innocently acquired (syphilis insontium). They occur about the lips, on the nose, chin, brow, cheeks, eyelids, and conjunctivæ; on the gums, the tonsils, and at other sites within the buccal cavity; on the fingers, most often of nurses and physicians; on the breasts; and, rarely, on the extremities.

*Varieties.*—Chancres vary as to the extent and form of ulceration (simple fissures, small ulcers, giant ulcers), the depth of ulceration (erosive, ulcerative, and boring chancres), the characters of the surface (papular, squamous, diphtheroid, pustular, and papillomatous chancres), and the character of the base (foliaceous, parchment, hypertrophic, elevated, and elephantiac chancres).

*Course.*—With the appearance of the eruption retrogressive changes in the chancre itself usually begin; they may set in earlier or be much delayed. The induration diminishes, the central portions of the chancre undergo fatty or ulcerative degeneration, and finally the sore disappears. Absolutely no trace of the lesion whatever may be left behind, particularly if it be situated on a mucous surface. As a rule, however, an indurated scar persists and may last for years; not infrequently the scar is pigmented. If the sore becomes infected or assumes a phagedenic character its clinical course is obviously altered. Prognosis as to the severity of the syphilis is by no means to be made from the character of the sore.

*Histology.*—The most notable findings are the enormous cellular infiltration and the marked changes in the bloodvessels. The infiltration originates in an exudation of lymphoid cells from the capillaries, and this is accompanied by a proliferation of the cells of the cuticular connective tissue and of the elements of the walls of the bloodvessels themselves. Mast-cells also occur. In the midst of the cellular infiltration the elastic tissue disappears. The new formation of cells extends along the small arteries and veins; the tissue becomes crowded with cellular infiltration and sclerosis soon takes place.[1] Meanwhile, thickening of the media, and proliferation of the intima

[1] Unna and others hold that the chief change occurs in the *adventitia.*

have occurred in the arteries and veins; so that the vessels, crowded by cells from without and blocked by proliferating endothelium from within, become narrowed in their lumen and sometimes completely obliterated. Poor circulation results, infiltration does not advance, and retrogressive metamorphosis begins. The vascular changes are very marked in the veins and in the lymphatics, the former being represented by rings with thick and rigid walls. The arteries also have thickened walls and their lumen is much diminished; all trace of elastic tissue disappears from the vessels. The lumen and walls of the capillaries of the papillæ often remain normal. The lymph spaces remain large. Giant cells and large epithelial cells occur; and Berkley has observed alteration in the nerve fibers going to the part. The epidermis over the chancre may be nearly normal; but the epithelial stratum is usually infiltrated, and often thinned and eroded. The formation of new cells occurs also in the papillary layer, starting from the blood-vessels; the papillæ are usually long and broad; and the interpapillary ingrowth of epithelium is often interspersed with proliferating young cells. In retrograding chancres fewer cellular elements are found, but many shrunken, connective-tissue shreds. The formation of the lymphatic cord running from the initial sclerosis up the penis superficial to the dorsal vessels may have important relation to the spread of the disease from the chancre.

*Diagnosis.*—The sharply defined borders, the induration, the slight sensitiveness, the scanty, non-purulent secretion, and the motility are the typical clinical features of the Hunterian chancre; but no one of them is invariable and the diagnosis of the sore is usually difficult, very often impossible, and as a rule not to be made, aside from finding the *Spirochæte pallida* microscopically, until sufficient time has elapsed for the appearance of secondary symptoms. The chancroidal ulcer and the lesions of herpes progenitalis offer the greatest difficulties in diagnosis of genital chancre. Other genital lesions which may be confused with chancre are secondary syphilides exhibiting ulceration, suppurative folliculitis, erosive balanitis and vulvitis, and certain of the tertiary syphilitic lesions. The appearance of these is, however, usually not typical of Hunterian chancre; the history is often helpful; and microscopic examination of smears will eliminate the non-luetic lesions.

The diagnosis of extragenital chancres offers greater difficulties. Here the position of the lesion instead of attracting one's attention immediately to syphilis may throw one off one's guard. The characteristics of the Hunterian sore are, however, usually to be found, and one should look particularly for the accompanying adenopathy. Chancres of the skin may be mistaken for pustular ecthyma and for tuberculous ulcerations. In the pharynx one may suspect diphtheria; on the fingers, lips, tongue, and tonsil differentiation from carcinoma is often difficult. Extragenital chancres may also resemble ordinary inflammations (*e. g.*, panaritium, abscess of the tonsil, etc.).

*Prognosis.*—In itself the chancre is usually benign; if ulcerative or phagedenic in character, however, it may in itself be a grave affection by reason of its effect on general health and of the loss of substance which it brings about. In certain situations, too, its nature is more serious; urethral chancres for example, lead to stricture and nasal chancres to atresia of the nostrils. The supposed increased gravity of extragenital chancres is probably due,

to other factors than the intrinsic nature of the lesion itself (*e. g.*, mistaken diagnosis and insufficient treatment, accompanying secondary infection, etc.).

**The Secondary Stage.**—The initial lesion is the clinical expression of syphilis in its primary and localized form. We do not know that the infecting agent has actually remained at the site of original inoculation or in the lymphatic glands nearby; what we *do* know is that during the first few weeks of the disease (the so-called second incubation period), no manifestations other than the local one, are to be observed. After a lapse, however, of about four to eight weeks from the appearance of the chancre the disease changes rather suddenly from a local to a general one; constitutional signs and symptoms, in great variety, appear; and this appearance marks the onset of the secondary stage of the disease. To this stage no terminal limit can be set; sometimes it lasts a few weeks, at other times many months; its course is greatly influenced by treatment; and if the disease is not well treated it may either pass directly into the tertiary form, or disappear entirely to reappear, after the lapse of months or years, as tertiary syphilis.

The symptoms of secondary syphilis are in a general way those of a more or less grave acute infection; but a large and motley group of specific symptoms is also superadded. The most characteristic of the latter are the lesions of the skin and mucous membranes; these are also quite often the most apparent manifestations as well as the first to appear.

1. *Symptoms of an Acute General Infection.—General constitutional disturbances* are usually present, often marked and in striking contrast to the feeling of well-being during the primary stage. There is loss of weight and strength; the patients feel badly and this condition may be exaggerated by anxiety over the nature of their disease. The appetite becomes poor, extreme anorexia being occasionally observed. In nervous women, however, boulimia is sometimes seen. Headache is a frequent, characteristic, and troublesome symptom. Usually it is described as a deep heaviness present most of the time, but much worse in the evening. Sometimes it is violent, almost intolerable, and quite prevents participation in the activities of life. The tonsils are often swollen independently of the occurrence of mucous patches. Sore throat is frequently complained of (angina erythematosa syphilitica). When the angina spreads to the uvula and soft palate the picture is characteristic and almost pathognomonic. The inflamed area itself is dark crimson, and is abruptly separated from the healthy mucosa anteriorly by an absolutely sharp border. The lingual tonsils may be swollen and dysphagia result. The spleen is sometimes enlarged, and this fact, if fever and roseola suggest typhoid fever, may add confusion to the diagnosis. Occasionally jaundice is present. Albuminuria is not frequent, but an interesting form of true nephritis occurs, which will be fully discussed under Visceral Lesions. Anæmia is a feature of the secondary stage; it is usually of the chlorotic type and may be attended by definite clinical symptoms (cardiac palpitation, sense of oppression, etc.). The details of the blood picture are described above. In neurotic individuals syphilis often causes an extreme exaggeration of the symptoms previously present. Intense psychic depression is not at all rare; pains in the limbs and analgesias and anæsthesias (particularly of the breasts in females) are seen, and sometimes the patients suffer from definite convulsive attacks. The patella reflex may be abolished.

*Enlargement of the lymphatic glands* is one of the characteristic features of secondary syphilis. It is not a local affair, like the adenopathy attending genital or extragenital chancre, but is an expression of general infection. The glands are not large, are indolent, painless, hard, discrete, unaccompanied by neighboring lymphangitis, and do not suppurate. The intensity of the glandular involvement is not proportional to the severity of the disease; on the contrary, marked glandular swelling usually accompanies mild lues, and vice versa. The most frequent lymphatic glands to be involved, arranged in order of predilection, are the postcervical, the sternomastoid, the submaxillary, the epitrochlear, the axillary, and the inguinal. Enlargement of the epitrochlears is particularly suggestive, since its involvement in other conditions is not very frequent. Involvement of a small gland just under the outer border of the pectoralis major has been considered almost pathognomonic of lues; the gland is certainly rarely involved in cases of acute infectious processes (phlegmon, etc.), since it lies off the drainage tract of parts oftenest so affected. Recently, however, such an enlarged gland was removed for purposes of diagnosis and found to be tuberculous. Enlargement of the inguinal glands is of little diagnostic value; it is by no means always seen in syphilis, and is very often seen in other conditions. Palpable and even enlarged lymphatic glands in this region are, indeed, almost a constant finding in patients seen in a genito-urinary out-patient clinic, and Dietrich has found that out of 499 healthy individuals 99 per cent. showed enlarged lymph glands somewhere in the body.

*Fever.*—Fever is a frequent phenomenon of the secondary stage and is one of the features of its resemblance to an acute infectious disease. At the end of the fifteenth and during the early years of the sixteenth centuries, when syphilis assumed epidemic proportions, its diffusion was so rapid and widespread that it was compared with smallpox (owing probably to the intensity and persistence of the cutaneous features), and hence the name variola magna, the great pox, or *the* pox. Fever was noted by many of the writers of this period—Massa, Vigo, and others. The great reformer, Ulrich von Hutten, whose *de Guaiaci* (1519) is the most interesting personal record of syphilis in the sixteenth century, must have been much plagued by the fever of the disease, as he personified it in two of his famous dialogues, *de Febris.*

Until the introduction of the thermometer no accurate clinical studies were made upon the subject, and the statement of John Hunter, "This fever has much the appearance of rheumatic fever and after a time partakes a good deal of the nature of the hectic" (1786), expresses the extent of our knowledge. Guntz (1863), a pupil of Wunderlich, was one of the first to study this feature carefully. Important papers have been published by Yeo, Phillips, Bristowe, and Parkes Weber in England; by Musser, Janeway, Futcher, and Birt in America; and by Baümler and F. Klemperer in Germany.

The frequency of fever during the course of syphilis is variously estimated. A large majority of all cases have a slight elevation of temperature at the period of incubation. Throughout its course the disease may be afebrile, and patients with the most extensive lesions may have normal temperature.

The fever occurs at three periods—preliminary, stage of invasion, and at any time during the tertiary lesions:

1. *Preliminary Fever.*—During the period of incubation of from eight to nine weeks the patient may be without symptoms, but there may be a

feeling of weakness and loss of appetite, with pallor. In a few instances at this period fever occurs. It may be ushered in by a chill (Lang) and be accompanied by headache, nausea, and pains in the limbs.

2. *Fever of Invasion.*—As a rule, by the time we see the patient in hospital the fever has disappeared. No large statistics are available, but various estimates give the proportion of cases with fever at from 25 to 35 per cent. It is probable, if we had accurate measurements, that slight fever would be found in a much larger proportion. It may antedate the eruption by a week or two and may set in abruptly with a chill. It is commonly associated with headache, malaise, and a furred tongue. The type of fever is usually remittent. Where malaria prevails the case may be confounded with the æstivo-autumnal type of this disease.

Much less frequently the fever of invasion is frankly intermittent. No case of this type at this period of the disease has come under our observation, but Fournier refers to it. The pains in the limbs and about the joints, with the slight fever, may lead to the diagnosis of acute rheumatism. A remarkable case of this kind was seen in a young woman of good family, who had been confined to bed for three or four weeks with pains in the joints and slight fever. She had irregularity of the heart's action and it was for this that the writer was consulted. The case turned out to be one of secondary syphilis following a chancre on the lip. In a young student, fever with the unusual complication of parotitis occurred during the stage of eruption. At this stage the picture may occasionally simulate typhoid fever, which Fournier describes as "*Typhose syphilitique.*"

3. *Fever of the Tertiary Lesions.*—It is particularly at this period that the presence of fever may lead to serious errors in diagnosis. The profession scarcely realizes that protracted fever of almost any type may occur in tertiary syphilis. It is probable that many of the cases of obscure, unclassifiable fevers which are described from time to time are due to latent syphilitic lesions. A man may have quite extensive gummatous disease of the liver without pain or without great enlargement. On the other hand, there can be no question that the most extensive tertiary lesions may be present with a normal or with a very slight elevation of temperature. Among diseases for which the fever is apt to be mistaken are:

*Rheumatic Fever.*—Nodes growing close to joints may cause peri-articular enlargement with pain, and if fever be present the case may be regarded as one of acute rheumatism. A girl aged nineteen years was admitted to hospital supposed to have rheumatic fever. The elbows, one wrist, and both knees were involved. There was slight elevation of temperature and a day or two elapsed before the true nature of the case was recognized. The presence of nodes on the clavicles and a more careful examination of the joints led to a correct diagnosis.

*Malaria.*—It seems scarcely possible that the two diseases should be mistaken, and yet in the case reported by Sydney Philips there were ague-like chills and the temperature curve was most suggestive. In one of our cases, reported by Futcher, a physician, aged fifty-nine, had chills and fever which he himself regarded as malarial, but it had resisted all treatment with quinine. When stripped, the diagnosis was easy, as he had a rupia-like eruption and tender nodes on the shoulders and sternum.

*Typhoid Fever.*—Cases have been reported in which the syphilitic fever has been mistaken for typhoid. They are rare, however, as J. D. Rolleston

states that out of a total of 3076 cases admitted to the London Fever Hospitals wrongly certified to be typhoid fever, only 10 were subsequently found to have syphilis. For weeks the following case, reported in Futcher's paper, was suspected to be typhoid fever: The patient, aged thirty-nine years, had had irregular fever for three weeks previous to admission. The temperature chart here annexed (Fig. 20) shows an intermittent and remittent fever from August 8th until September 16th. He had a furred tongue. There were no malarial parasites. The spleen was enlarged. A continuous fever of this character in the autumn which resisted quinine was naturally regarded as typhoid. It was not until September 12th that suspicion was aroused and W. S. Thayer noted the presence of thickening of the clavicles from old nodes. There was a definite scar on the glans and the patient acknowledged infection. Potassium iodide was given at once and by September 16th the temperature was normal. It remained so and he was discharged October 3d perfectly well.

*Tuberculosis.*—Perhaps more important than any of these is the simulation of pulmonary tuberculosis by syphilitic fever. Many writers have called attention to these cases, and E. G. Janeway brought a series before the Association of American Physicians in 1898. The question of the relation of the two diseases has been considered in a monograph by Sergent.[1] It is more particularly in the form in which there are sweats, irregular hectic fever, and loss of weight, associated with a slight cough, that tuberculosis is suspected. The absence of well-marked physical signs and of bacilli in the sputum may suffice to call attention to the anomalous nature of a case. The liver is very often enlarged, irregular, and tender, and it is this feature that may suggest the proper treatment, which is, as a rule, followed by prompt recovery.

It is by no means easy to see why in some cases fever is present and absent in others. In many instances the liver is involved and it has been suggested that the damage to this organ is sufficient to prevent its proper action as a filter, and in consequence fever-producing substances reach the general circulation. As with other microörganisms, the spirochæte produces toxins to which the fever probably represents a natural reaction. In a few cases gummata become secondarily infected by pyogenic organisms, but this is exceedingly rare.

2. *Specific Symptoms of Secondary Syphilis.—Syphilitic arthritis* is very frequently complained of. It usually takes the form of dull pains in the joints of the extremities—much like the "growing pains" of children, or of "rheumatism," and is frequently regarded by the laity as rheumatic in character. The joints are usually not swollen, tender or red, although a small effusion may be present. The pains are as a rule not severe, but are worse at night and may be intense. They persist for a longer or shorter period, then disappear without apparent cause, and often return at irregular intervals. They resist all measures except specific treatment. More characteristic still are the osteocopic pains in the periosteum of the long bones; the clavicle, sternum, tibia, and humerus are most frequently affected. When the bones of the head are involved the dull, remittent headaches occur. These pains are usually worse at night and are out of all proportion to objective signs; the latter are as a rule absent, although there may be swelling of the periosteum

[1] *Syphilis et tuberculose*, Paris, 1907.

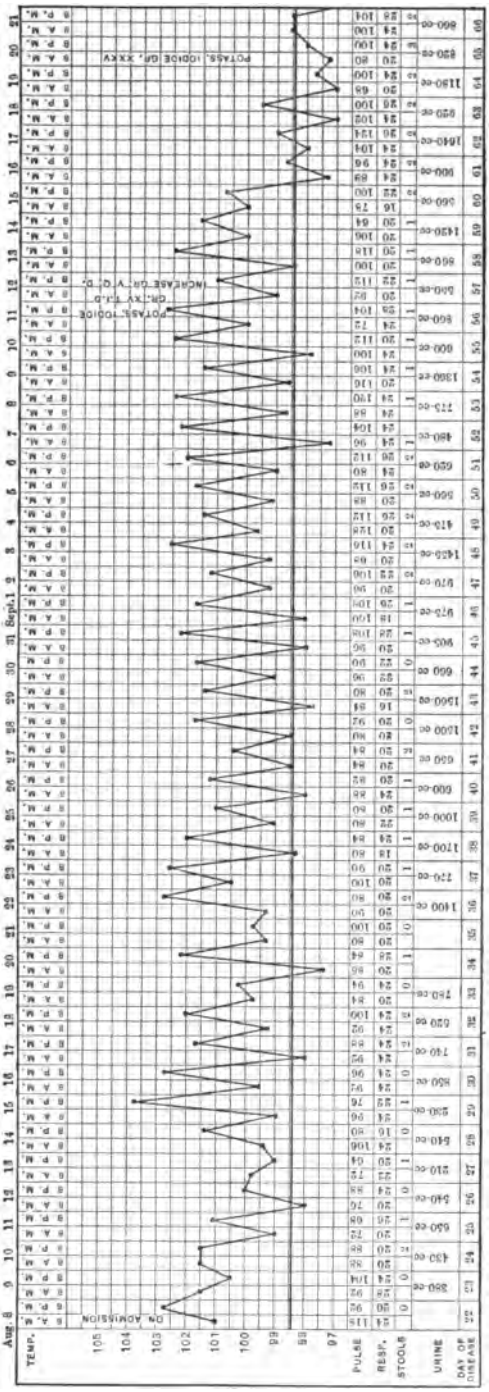



Fig. 20

Fever curve suggesting typhoid fever.

and even a definite periostitis. The muscles and joints are often stiff and sore.

*Ocular symptoms* are often present. The most frequent of these is iritis. At first only one eye but finally both are involved. The iritis may be plastic, serous, or gummatous. The third form alone is peculiar to lues. It is accompanied by all the signs and symptoms of ordinary iritis. In addition one or more yellowish or yellowish-red, nodular elevations are seen, varying in size from a hemp seed to a small pea. They are situated in the pupillary margin, on the ciliary border or between the two, but they tend to coalesce. The prognosis of the condition is doubtful on account of the frequent formation of posterior synechiæ.

*Disturbances of the nervous system* are frequent and of the gravest import. They are sometimes responsible for death during the secondary stage. Their full treatment belongs to neurology and they will be dealt with subsequently. The most serious involvements are due to the acute arteritis so characteristic of the disease, thrombosis of the cerebral arteries with softening being a not infrequent occurrence. Actual rupture of a syphilitic artery (the frequent cause of apoplexy in the young) is usually a phenomenon of the tertiary stage, and is due to a gummatous change in the vessel wall. Acute meningomyelitis, peripheral neuritides, and compression paralysis due to periosteal lesions, are fairly common.

Functional disturbances are not uncommon. Fenger and others have shown that the skin and tendon reflexes are first increased and then depressed, sometimes finally disappearing.

*Visceral lesions* are so much more characteristic of tertiary lues than of secondary that they are all described together below. There are, however, sundry symptoms occurring in the secondary stage, which are undoubtedly due to some pathological change in the viscera and which may run imperceptibly into the tertiary symptoms which arise from gummatous inflammations. The bone symptoms are an example. In addition to the "rheumatic" pains already described, a periostitis with the appearance of painful and tender nodules is not uncommon; and an ostitis with the formation of exostoses is occasionally seen, particularly in the tibia. So, too, there may be arthritis with effusion, which may even be polyarticular and resemble acute articular rheumatism. Serous exudation is also seen occasionally in the tendons and bursæ. The involvement of the liver in some pathological change is probably to be inferred from the jaundice which sometimes appears early.

*Cutaneous and mucous lesions* are the most characteristic and constant manifestations of secondary syphilis. Nowhere is the wanton nature of the disease more obvious than in its skin lesions; for there is hardly a single cutaneous affection which lues may not simulate. The cutaneous syphilides, however, have certain common characteristics which distinguish them in part or in whole from other skin diseases. These are as follows:

(*a*) The syphilitic lesions are usually circular or approximately so.

(*b*) Their evolution is slow and the successive crops of eruption are dissimilar.

(*c*) They are more or less symmetrical in their distribution, showing a tendency to grouping, particularly in circles and semicircles.

(*d*) They have a characteristic reddish-copper color, which resembles raw ham.

(*e*) They are usually indurated and often present at the periphery a raised collarette (the collarette of Biett).

(*f*) They usually cause no itching or other subjective symptoms, although in occasional cases pain is marked.

(*g*) They tend to resolve, although often leaving behind them scars, not infrequently pigmented. (In the precocious malignant syphilide, rapid ulceration with extensive tissue destruction occurs.)

(*h*) They tend to become generalized and to involve large areas of skin. When localized, they have certain seats of predilection—the forehead (corona veneris), the extremities, the anogenital region, etc. The dorsal surfaces of hands, wrists, and feet are exempt, and the sternal and clavicular regions are rarely involved except in the late destructive lesions.

(*i*) The scales are thinner, more superficial and less abundant than those seen in non-luetic lesions; they are dirty gray and do not glisten.

(*j*) The crusts are gray, greenish brown, or black; they are made up of superimposed layers; the surfaces are rough and laminated, and they are more easily detached and thicker than in non-syphilitic lesions.

(*k*) The ulcerations tend to be kidney or horseshoe shaped.

(*l*) The lesions are altered by climate, age, sex, alcoholism, and the presence of so-called "diatheses." This is particularly marked in seborrhœic individuals, in whom the luetic eruptions often take on seborrhœic characteristics (the "interlocking of seborrhœa and lues" of Unna). This characteristic is known as syphilitic imitation.

(*m*) Finally, they are polymorphous, often manifesting themselves simultaneously in various forms.

The cutaneous syphilides may be classified as follows:[1]

1. The erythematous form
   - Macular
   - Maculopapular
2. The papular form
   - Miliary
   - Lenticular
   - Papulosquamous
   - Moist papular
3. The pustular form
   - Varicella or variola variety
   - Acne variety
   - Impetigo variety
     - Confluent
     - Rodent (with deep ulceration)
   - Ecthyma variety
     - Superficial
     - Deep
   - Rupial variety
4. The tuberculous form
   - Tuberculous
   - Gummatous
5. The serpiginous and vegetating forms
6. Extravasation forms
   - Extravasation of pigment (pigmented syphilide)
   - Extravasation of blood (purpuric syphilide)

The names of certain of these lesions explain their nature; the other more characteristic cutaneous syphilides will be described.

(1) *Syphilitic Roseola.*—The secondary stage is oftenest inaugurated by the appearance of a measly, roseolous rash, and this event may be said to end

[1] Cazenave's modification of Biett's classification is followed, with a few slight changes.

the second incubation period. It takes place about the forty-fifth day after the appearance of the chancre. The rash usually appears first on the flanks and the sides of the thorax; thence it extends to the trunk and the extensor surfaces of the limbs. The face and hands are, as a rule, not involved. The rash consists of small, flat, usually round or oval macular spots. They are all of about the same size and are widely disseminated. At first they are rose-colored, later becoming darker, wine-colored, and finally fading into a pinkish yellow. Pressure makes them disappear only in the early stages. If observed through blue glass, as advised by Broca, the macules always become more apparent, and they may be recognized in this way when not otherwise visible. Occasionally the lesions are somewhat raised, like the wheals of urticaria. The rash, unlike the exanthemata of acute fevers, comes out slowly; it then persists for several weeks and finally gradually disappears. In some cases its whole course is a rapid one. Recurrences are not infrequent, and luetic patients may exhibit repeated macular eruptions at intervals even of years.

The diagnosis of syphilitic roseola from other macular cutaneous affections sometimes presents a good deal of difficulty. Measles and pityriasis rosea are the two diseases most frequently to be differentiated from syphilis. As a rule the history, the nature of the accompanying constitutional and other disturbances, and careful examination of the lesions for the specific luetic characteristics will make the diagnosis. The frequent involvement of the face in the rash of measles and its rare involvement in syphilis is an important point in the differential diagnosis. Other acute exanthemata, medicinal rashes, the eruptions of typhus and typhoid, erythema, and the roseola of gonorrhœa may also be mistaken for the macular syphilide.

(2) *The Papular Eruption.*—This represents the second stage in the evolution of the cutaneous syphilide. It usually follows the roseola by a short interval, but in some instances it comes out before the latter has disappeared; and its appearance may, on the other hand, be much delayed. The eruption consists of round, or nearly round, reddish, raised papules, varying in size from a lentil to a ten-cent piece. The lesions may be quite intact, but are often covered with a slightly squamous epidermis. They are situated most often on the trunk and face. Not infrequently they lie arranged in groups around a central element (syphilide papuleuse en corymbes of the French). The miliary or lichenoid form of papule deserves special description. When appearing early the lesions are very numerous and usually uniformly distributed; the abdomen, back, limbs, and face may be covered.

In its late form, the papular syphilide appears generally three or four months after the onset of the disease and the lesions are much less numerous. It is a polymorphous eruption, but the lesions are in general miliary and of a reddish-brown color. They are not infrequently capped by a small pustule, or covered with a crust or a scale. They are arranged in groups, often like constellations. Another more special form of papular syphilide often seen and of great interest from a diagnostic standpoint is the badly named syphilitic psoriasis. Here the lesion is a large copper- or ham-colored one, occupying a large extent of body surface (face or limbs). The edges are often indistinct, and the lesion consists of numerous concentric circles. On the surface the epidermis is partly detached in the form of dirty, dry scales, which may be easily removed without bleeding. Fissures and rhagades often accompany this syphilide, and its resemblance to ordinary psoriasis

is obvious; but the localization, the rapid evolution, the influence of specific treatment and the appearance of the scales, together with the general clinical features of the case, are usually sufficient to make the diagnosis.

The large papular or lenticular syphilide is quite commonly seen. It shows a predilection for sites about the natural orifices of the body; but is also seen on the neck, trunk, chin, and palms. It may appear at any time in the secondary stage and be the only cutaneous manifestation. Often it occurs simultaneously with the mucous patches. The lenticular papule is the most common and characteristic of the papular eruptions. The lesions are round or oval, with sharp borders and slight elevation. At first they are small and red, but later become copper-colored. The surface becomes shiny, the lesion breaks at its centre and desquamates. The desquamation is repeated until finally the lesions disappear, leaving behind them brownish or bluish-gray spots. The eruption usually starts on the forehead (corona veneris), or the nape of the neck; it then spreads to the abdomen and in two weeks is pretty well generalized. It comes out in crops and may last for ten months.

The papular rash sometimes becomes *nummular*. Here the lesions are large, with marked umbilication and a tendency to desquamation. Later they become annular, with a ring-shaped periphery of induration persisting. Intersection and interfusion of such circular, semicircular, and elliptical patches gives a dreadful and bizarre appearance.

The secondary papular syphiloderm of the palms and soles (psoriasis palmaris et plantaris syphilitica) appears as lentil-sized, non-elevated, brownish spots, which are indurated and evolve slowly. When retrogressive changes begin, a white, glistening scale forms at the centre, surmounting a smooth, reddish depression. A collar of semidetached scales forms around the papule and a brown stain is left after the disappearance of the lesion. Fissures and ulcerations are not uncommon. The syphilide is chronic in its course, obstinate to treatment, and frequently relapses. It is pathognomonic of lues, but must be distinguished from eczema and, rarely, from psoriasis.

The moist papule or broad condyloma occurs where the lesion is exposed to warmth or maceration. Neglect and uncleanliness favor its development. It appears as a flat, button-like excrescence, often much elevated above the surrounding skin; its surface may be papillary, is denuded of epithelium, and covered by a layer of dirty, grayish material, which is usually bathed in a foul, thin secretion. Condylomata are much commoner in women than in men. The lesions are most often bilateral and are extremely infectious. They hypertrophy, particularly when neglected, and may then coalesce, forming extensive, flattened, mushroom excrescences. Condylomata occur most often about the anus; but they are also frequently seen on the vulva, perineum, scrotum, thigh, etc. They are very liable to recur frequently. The diagnosis is, as a rule, easy.

(3) *The Vesicular Syphilide.*—This form is excessively rare and is ephemeral when it occurs at all, being soon replaced by crusts. Small vesicles are sometimes seen in connection with the miliary papule. It is doubtful if true bullæ ever occur.

(4) The *pustular syphilide* is, on the whole, rare in the secondary stage of the disease, and its occurrence then usually indicates a severe type of the disease. It occurs most often in cachectic or debilitated subjects. It is the latest of the secondary eruptions, is obstinate to treatment and prone to

relapse. The pustules vary in size from small, acuminated, acne-like lesions to large, pustulocrustaceous forms. Syphilitic polymorphism is well exhibited by the pustular syphilide, the lesions varying in size, number, distribution, and extent of suppuration. The lesion may resemble any of the pustular skin diseases (acne, ecthyma, varicella, impetigo, etc.); but two clinical forms, the small and the large pustular syphiloderm, should be recognized.

The small pustular syphiloderm resembles acne in many respects. The lesions, which develop from papules, are small, grow slowly, and often remain stationary for weeks, drying up finally into yellow crusts. In the early form the pustules are very numerous and are well scattered over the body. In the later forms they tend to be grouped on the scalp, elbows, knees, etc. Successive crops of small pustules often follow one another for months. In the diagnosis the distinction from acne, variola, and varicella offers the chief difficulty.

The large pustular syphiloderm begins as the large lenticular papule, which rapidly becomes pustular; the pustule soon ruptures or dries up into a crust, removal of which shows an ulceration beneath. When the ulceration heals a brown, pigmented scar is left behind. The lesion, however, usually lasts for a long while, the crusts heaping up to form the rupia syphilitica. This rupial eruption is frequent and striking. It begins as a flat papule, which becomes bullous or purulent, and is surrounded by a livid inflammatory areola. The pustule ruptures and the contents dry into brown or black crusts under which ulceration continues. The crusts, in this way, become stratified and thickened (oyster-shell appearance). The base increases in size and the lesion in height, becoming finally cone-shaped. If the crusts are removed an indolent ulcer is exposed with abrupt, undermined edges, and containing serosanguineous pus. The differential diagnosis between the large pustular syphiloderm and variola is sometimes very difficult. The syphiloderm, however, makes its appearance more slowly, begins upon the trunk and not upon the face, and shows the concomitant signs of lues.

It is not certain whether the pustular syphilide is the result of an actual secondary invasion or not. Unna has shown that such an invasion is very rarely demonstrable.

(5) The *tuberculous* and *ulcerated syphilide* merges into the papular syphiloderm on the one hand and the gumma on the other. It does not usually appear until about two years after the initial sore. When occurring early it signifies a grave form of the disease. The lesions are circumscribed, brownish-red, bean- to walnut-sized infiltrated tumors, usually relatively few in number and tending to be grouped, particularly upon the nose and forehead. The course is chronic, the lesions disappearing either by absorption or ulceration. When the lesions are few and situated on the face the similarity with lupus vulgaris may be very striking.

The ulcerated syphilide is either the subsequent stage of the tuberculous syphilide or appears as a manifestation of the rapid malignant form of syphilis. The lesions appear as red, brownish tubercles, which soon soften and ulcerate. There is an irregular loss of substance, with suppuration. This may be extensive, causing great deformity. If the lesion heals, it persists for a while as a reddish infiltration, with a protruding border and covered by a crust. It may be 3 or 4 cm. in diameter. When it disappears it leaves behind it a marked scar, often with a surrounding area of pigment.

The lesion may be situated anywhere on the body, but is most often seen on the legs. It occurs most frequently in weak subjects and may follow the chancre immediately.

(6) *Pigmented Syphilide.*—This cutaneous lesion appears six to twenty-six months after the chancre; it is unique among the cutaneous syphilides in its resistance to specfic treatment; it is accompanied by no symptoms and is sometimes regarded as a parasyphilitic manifestation. It is most frequent in young patients and is oftener seen in women than in men. It is called by German writers syphilitic leucoderma and consists of large, non-elevated, confluent, grayish patches, enclosing circular or oval areas of normal skin among them. The general arrangement suggests lace with large meshes. The non-colored portions of skin appear, by contrast, whiter than normal skin. The rash is almost always situated on the sides of the neck and is symmetrically disposed; it is also seen in front of the axillæ, on the sides of the abdomen, and on the flanks. Occasionally it occurs on the entire body. It often occurs without having been preceded by any other eruption. Its pathology is not clear; Unna and the French consider the pigmented syphilide as a primary cutaneous manifestation of the disease; the Germans regard it as the remains of an old eruption.

(7) *Changes in the Hair and Nails.*—Alopecia is a frequent and well-known, although by no means constant, sign of secondary syphilis. It appears during the third or fourth month of the disease, and may be either general or circumscribed (alopecia alveolaris). At first single hairs fall out; later spots of alopecia, varying in size from a lentil to a silver dollar, gradually appear. There are no broken hairs in the spots—an important fact for diagnosis. The alopecia often occurs simultaneously with the pigmented syphilide of the neck. The eyebrows at the same time may be affected and sometimes fall out entirely. The hair is reproduced after syphilitic alopecia and the prognosis is, therefore almost invariably good. The fall of the hair is due to a folliculitis of the hair follicles; it is accompanied by decoloration of the deep portions of the hair and by a dilatation of the small vessels about the follicle. Changes in the nails are not infrequent. The nails may be cracked or hypertrophied; and often there is an accompanying involvement of the peri-ungual tissues (syphilitic onychia and paronychia).

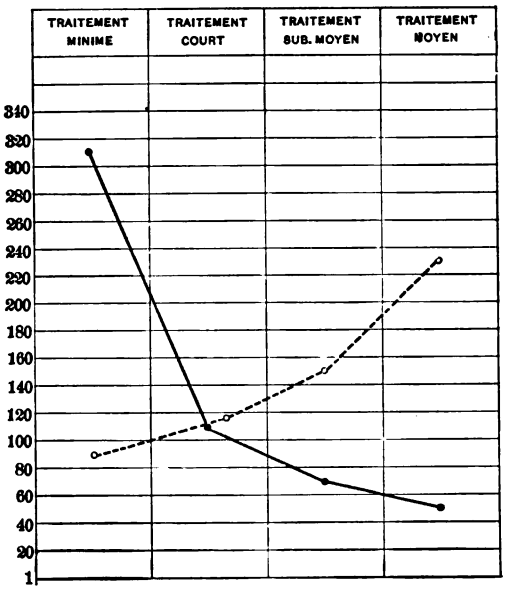
(8) *Lesions of the Mucous Membranes.*—These are among the most important and constant manifestations. On account of their extreme virulence they are a grave feature as regards the spread of the disease. All the lesions seen on the skin may also occur on the mucous membranes; but the most characteristic lesion is the well-known mucous patch. This is seen oftenest in the mouth and consists of a reddish or characteristically opal, slightly raised, papular area, topped by a small erosion. It occurs at various places in the buccal cavity, quite often on the tonsils; and is seen oftenest in mouths subject to some constant irritation like that of tobacco. When the mucous patch occurs on a site subject to mechanical irritation and to neglect (on the vulva, about the anus, etc.) its character changes and it is called a condyloma. It becomes larger, protrudes, is covered by fungous, papillomatous growths, and has an abundant, foul secretion. This may ulcerate and become diphtheroid. Mucous patches often recur many times during the course.

The mucous patches may become confluent and cover large areas. Rhagades and painful fissures are often associated with them. They may cause marked subjective symptoms. Mucous patches are to be diagnosed from

mercurial stomatitis, leukoplakia buccalis, and aphthous erosions. Their frequent occurrence on the tonsils and soft palate is an important point in diagnosis.

The macular, papular, and even pustular syphilides may be situated in the mouth. The angina syphilitica, of greatest interest on account of its clinical importance as one of the early signs of constitutional syphilis, is the most frequent of these buccal syphilides. It consists in a reddening of the tonsils, the pharynx, the uvula, or the soft palate, which is sharply defined anteriorly. It gives the patient little trouble as a rule. Syphilitic laryngitis is also not infrequently seen. In these cases the voice acquires a peculiar roughness which may progress even to complete aphonia.

FIG. 21




The dotted line represents the frequency curve of late secondary syphilis; the heavy line the frequency curve of tertiarism. (From Fournier.)

**Late Secondary Syphilis.**—This is a form of the disease to which Fournier has given special attention.[1] It consists of secondary phenomena manifested late in the disease, and of such cases Fournier found nearly 1100 examples in a series of 19,000 syphilitic patients. The symptoms may occur at any period of the disease, even so late as in the thirty-first year. What is most interesting is that the late secondary phenomena apparently occur most often in the cases which have been well treated, in direct contradistinction to the phenomena of tertiarism (Fig. 21). This of course does not contra-indicate efficient treatment, for it is the tertiary phenomena which are to be feared. Any of the secondary symptoms may occur in this form of the disease, but the following are most often seen:

[1] *Syphilis secondaire tardive*, A. Fournier, Paris, 1906.

(*a*) *Cutaneous Syphilides.*—Any one of the secondary eruptions may occur, but when seen in this late stage the peculiar feature of them is their attenuated, abortive character. The recurrent roseola, for example, consists of circumscribed, regional, discrete, large, pale, and tender lesions. Quite frequent, too, is the tertiary erythema, which consists of a single, very superficial reddening of the skin, without infiltration, and free from scales.

(*b*) *Iritis*, which is essentially a secondary phenomenon, may occur in the tertiary stage and even years after the chancre.

(*c*) Most important are the *mucous syphilides*, particularly those of the mouth, which, in the secondary form, occur with extraordinary frequency long after the secondary stage. *Glossite dépapillante* and many scrotal and genital syphilides are among the most common secondary mucous lesions seen in the late stage.

These phenomena are not in themselves serious; but they are particularly important from the standpoint of contagion. "Late secondary syphilis has for a corollary late syphilitic contagion." In view of these facts one should watch carefully the cases of benign recurring syphilis (with recrudescences of secondary manifestations), and particularly the cases complicated by nicotine stomatitis, which seems to be a determining factor in the occurrence of the glossitis so characteristic of late secondary syphilis.

**The Tertiary Stage.**—The secondary stage has no sharply marked terminal limit; but as it progresses the intervals of freedom from symptoms increase in extent and the symptoms themselves diminish in severity until finally an extended period of latency supervenes. This may, indeed, continue throughout the patient's life and mark the end of the disease; on the other hand, it may mean only an abatement of symptoms which, with the advent of the tertiary stage, again appear. On the average the phenomena of tertiarism appear about three or four years after the chancre; but they may, in precocious cases of galloping syphilis, be present at the end of a few months, and in others they succeed the secondary phenomena without any interval of freedom from symptoms. They may again appear as late as fifty-five years after the initial sclerosis, and in a fair proportion of cases they are wanting altogether. They may be preceded by any one of a group of Hutchinson's so-called "intermediate symptoms:" gumma of the testicle, psoriasis palmaris, choroiditis, arterial disease expressed in convulsions, visceral engorgement, nervous symptoms (retinitis, etc.), and rupia.

Just what determines the appearance of tertiary symptoms is not known. Certainly the absence of treatment, as Fournier so strongly insists, is an important factor; out of 2396 cases of tertiarism collected by him, 78 per cent. had not been treated at all, 19 per cent. had received moderate treatment, and only 3 per cent. had been properly treated. On the other hand, the gravity of the early syphilis bears no distinct relation to the probability of the appearance of tertiary symptoms; benign cases, and even cases without secondary symptoms, often pass through a typical and even a severe tertiary stage. Alcoholism and all conditions favoring lowered resistance seem to predispose to tertiary syphilis. In general the lesions of the tertiary stage are distinguished from those of the secondary by their lack of orderly appearance and progression, by their persistence, by their asymmetrical and local arrangement, by their relative non-infectiousness, and by their tendency to ulceration. Syphilis in this stage is also less transmissible to heredity than in the secondary stage.

**The Visceral Affections.**—These form a most important clinical group. They are not, it is true, absolutely confined to the tertiary stage, but as they are much more frequent then than at earlier stages, it is convenient to consider them together in this place.

I. **Syphilis of the Respiratory System.**—1. TRACHEA AND BRONCHI.—Tracheal and bronchial catarrh may occur in the secondary stage. Later there are more serious lesions, which while relatively rare have great importance from the fact that in almost every instance life is threatened, and the mortality in the whole group of cases is very high. L. A. Connor has recently studied the subject very thoroughly.[1] In an analysis of 128 recorded cases men and women were about equally affected. In 10 cases the lesions were ascribed to inherited syphilis. The average duration of the infection was about ten years; 97 of the cases came to autopsy. The lesions were: (*a*) *Gummata*, 20 cases; the lesions were sometimes single, in others the tumor extended over a considerable area of the trachea or involved the whole circumference; (*b*) *ulcers* were present in 44 per cent. of the cases, and as a rule were large and deep. In many cases the cartilages were eroded and fragments had been coughed up. Perforation of the trachea or of a bronchus occurred in 12 cases, in 5 with fatal hemorrhage. This group is very important with reference to the acute ulcerative perforation of large blood-vessels. In 2 cases an ulcer of the right bronchus perforated a branch of the pulmonary artery. In the case of Bernays, of St. Louis, a small ulcer of the trachea perforated the arch of the aorta. In Turner's case an ulcer just above the orifice of the right bronchus perforated the superior vena cava, and in Watson's case an ulcer of the left bronchus perforated a branch of the bronchial artery. In 2 instances the œsophagus was perforated. In several cases the ulcer perforated into the peritracheal tissues, with the formation of an abscess and once with tracheocele; (*c*) *endotracheal scarring and contractions;* in 40 per cent. of the cases there were scars, bands, or obliterative endotracheitis, with marked stenosis. In some of these cases ulceration seems not to have been a preceding condition, but a slow, progressive proliferation of the submucous tissues has led to gradual narrowing of the lumen; (*d*) *fibrous peritracheitis;* of this there were 8 cases in Connor's series. The trachea and the main bronchi are encased in a dense mass of connective tissue which had involved not infrequently the recurring laryngeal nerves. It is probable that these peritracheal lesions in syphilis start as gummata of the lymph glands between the trachea and the œsophagus, and finally lead to a fibrous peritracheitis.

The associated lesions are most important. Syphilis of the lungs was present in 10 cases. Dilatation of the trachea was present 3 times, in each instance above the point of structure. It is remarkable that bronchiectasis was not more frequent, only 20 per cent., considering that in all but about 15 per cent. of the cases obstruction of some sort existed.

*Symptoms.*—Cough, dyspnœa (often paroxysmal), and stridor are the special features of the condition. The expectoration is often blood-stained, purulent, and fetid, sometimes with fragments of the tracheal cartilages. Profuse hemorrhage, when it occurs, is usually from a large vessel and is promptly fatal. Progressive dyspnœa, one of the most constant symptoms, is usually associated with attacks of orthopnœa and cyanosis, which may

[1] *American Journal of the Medical Sciences*, vol. cxxvi, p. 57.

come on with great suddenness and rapidly prove fatal. This peculiar feature of paroxysmal, intermittent dyspnœa has attracted the attention of many writers on the subject. Grossmann and others regard this type of dyspnœa as an effect rather of cardiac insufficiency than of the actual stenosis. No symptom is more striking in the disease than the stridor, which is present in about 50 per cent. of the cases. It may occur with inspiration alone or with both acts. It may be of the loud, roaring character; more commonly it is of higher pitch and sometimes it is quite sibilant. Among other symptoms are pain, which is not very frequent, and tenderness over the trachea. Aphonia was present in some cases even when the larynx was normal. Retraction of tissues at the root of the neck during inspiration is not infrequent. Gerhardt called attention to the limitation of the vertical movement of the larynx in tracheal as an important differential sign from laryngeal stenosis.

The *diagnosis* is not often made in the cases without stenosis, unless ulcers and scars are seen in the trachea by laryngoscopical examination. With tracheal or bronchial narrowing the clinical picture is very definite: "(1) A peculiar type of dyspnœic breathing in which the prolonged, labored, and relatively slight inspiration and the shorter, easy expiration follow each other without the usual pauses; (2) a stridulous sound, chiefly or altogether inspiratory; (3) in most cases an inspiratory sinking in of the tissues of the root of the neck, the epigastrium, and the lower intercostal spaces" (Connor).

The *prognosis* of the disease is grave. The mortality among 128 cases was 76 per cent. In 11 of the cases death occurred in an attack of suffocative dyspnœa, in 4 it was due to hemorrhage. The *treatment* is not very satisfactory. In a few cases antisyphilitic measures have been successful. Schroetter has treated some cases successfully with dilatation, which has been practised even in narrowing of a main bronchus. Tracheotomy was performed in 17 cases of Connor's list, in only 2 with permanent improvement.

2. LUNG.—With the discovery of the specific organism we may expect more light on the difficult problem of pulmonary syphilis. All are agreed that the lungs are rarely attacked, few are agreed as to the distinctive features of the lesions, and fewer still as to the clinical symptoms.

Many of the old writers in the sixteenth and seventeenth centuries spoke of a phthisis originating in lues, but it was not until the latter half of the nineteenth century that the attention of pathologists was particularly directed to the subject. Depaul in France, Virchow and Wagner in Germany, were the first to describe the lesions in the congenital and acquired forms. The literature is very fully given by Flockermann[1] and Herxheimer.[2] Anatomically the disease is rare. Among 2500 autopsies at the Johns Hopkins Hospital there were 12 cases in which lesions believed to be syphilitic were present. J. K. Fowler, who has given us the best study of the disease which has appeared in English,[3] was only able to find 12 specimens in the London museums, and 2 of these were of a doubtful nature.

Clinically the disease is rarely recognized. In not one of the cases seen by the senior author in which the condition was suspected was it certain, and in none of these was the diagnosis confirmed postmortem. On the other hand, there are clinicians who believe that a great many cases which we regard

[1] *Centralblatt f. allg. Path.*, Bd. x.
[2] Lubarsch und Ostertag, *Ergebnesse*, Jahrg. xi, 1907.
[3] *Diseases of the Lungs*, London, 1898.

as tuberculous have in reality a syphilitic origin. The difficulty in reaching the conclusions as to the nature of a case may be gathered from the fact that of Hiller's 84 collected cases with autopsies, Councilman regards only 28 as shown to be definitely syphilitic. It is more convenient to consider the congenital and acquired conditions separately.

*Congenital Pulmonary Syphilis.*—Gummata are exceedingly rare. The common lesion is the so-called *white pneumonia.* Virchow described in the lungs of stillborn children a diffuse change, sometimes involving all the lobes and causing a marked consolidation with great increase in volume, so that the pleural surface showed the impression of the ribs. The cut surface was dry, grayish or yellowish white in color, and smooth, and it has been called "pancreatization" from the similarity of appearance to a section of the pancreas. While the children, as a rule, are stillborn and premature, yet, sometimes they are born at term and they may live for several hours. In other cases or in other parts of the same lung the surface is less uniform, and presents a more grayish tint, and is firmer, indicating that sclerotic changes have occurred. This so-called interstitial pneumonia is only an advanced stage of the other process and is due to the great increase in the alveolar and interlobular connective tissue. Sections prepared by proper methods show in these lesions an extraordinary number of spirochætæ. While the majority of all cases of congenital pulmonary syphilis have only an anatomical interest, there are a few cases in which the lesions have appeared later in life; but it may be very difficult to determine the exact nature, as the co-existence of tuberculosis with syphilis in young infants is by no means uncommon.

*Acquired Syphilis.*—The lesions may be described as follows: (1) *Gummata* are rare and involve, as a rule, the neighborhood of the hilus and the lower lobes. They have the usual appearances of these structures and vary in size from a hazelnut to a hen's egg. They may soften and break into bronchi, or they may undergo sclerotic changes leading to extensive shrinkage of the lung tissue and to bronchiectasis. (2) *Bronchopneumonia.* Orth and others regard an exudative syphilitic pneumonia as very doubtful. New investigations should now be able to determine this point. The case recorded by Délèpine and Sisley[1] shows one way in which the lung may be involved. An enormous gumma of the right lobe of the liver, measuring five and one-half by four and one-half inches in extent, pushed up the diaphragm, to which it was firmly adherent, and extended through and involved the lower lobe of the lung. There were patches of caseous pneumonia and others looking like catarrhal pneumonia. With these there was sclerotic induration. The specimen, one of the most remarkable ever described, is well figured in Rolleston's work on the liver. In this case the involvement of the lung was by direct extension and the lesion was in no respect an ordinary bronchopneumonia. It is not yet proven that the diffuse infiltration of a lobar or lobular character recorded by Rollett, Schnitzer and Aufrecht, and others is in reality syphilitic. (3) *Sclerotic patches, chronic interstitial pneumonia.* At the root of a lung, more particularly, but scattered anywhere throughout the tissues, sometimes mapping out a large group of lobules, or radiating from the hilus of the lung, are long strands of fibrous tissue fissuring and dividing the organ, the pulmolobatus of Virchow. In advanced

[1] *Pathological Society Transactions*, London, xlii.

cases bronchiectasis occurs, or there may be cavity formation. When these scars occur alone, without gummata in the neighborhood and without signs of syphilis elsewhere, it is impossible to determine their exact nature. On the other hand, when such lesions co-exist with gummata, or when they actually surround or extend from them, the syphilitic character is evident.

*Clinical Features of Pulmonary Syphilis.*—A few well-marked cases have come under personal observation. In the following the pulmonary features were in the background and the patient died of an interstitial nephritis:[1] M. T., white, married, aged forty-three years, entered the hospital October 6th, complaining of shortness of breath and œdema of the lower extremities. The patient had usually enjoyed good health. She had had acute rheumatism several times, the first attack eight years ago, and since then several other attacks, the knees being principally affected. She has been short of breath for the last two years. Of late this has increased and she had a good deal of cough. Swelling of the legs began in July and increased very much in the two weeks before admission into hospital. On physical examination there was slight dulness in the posterior portion of the lungs and numerous moist rales at both bases posteriorly. On the face and right infraclavicular region were several nodules of ecthyma. On the 13th the patient had a chill. The examination of the urine showed a large amount of albumin and numerous casts. The patient died October 24th. At the autopsy chronic nephritis, heart hypertrophy, and a syphilitic liver were found.

Microscopic examination showed amyloid infiltration of the liver, spleen, and kidneys. This widespread amyloid degeneration, with the characteristic gummata of the liver and bands of fibrous tissue, left no doubt as to the correctness of the diagnosis of syphilis. The condition of the lungs was remarkable, a typical pulmolobatus. The surface of the right lung was very irregular. It was divided into large projecting portions with deep depressions between them. At the bottom of these depressions the pleura was thickened, and there were bands of connective tissue running from the thickened pleura toward the centre of the lung. Some projecting areas of the lung were almost cut off from their connection. The alveoli in these portions were plainly visible to the eye, and the lung substance was very atrophic. All of the projecting portions were emphysematous, some more than others. On section there were dense masses of connective tissue along the bronchi and great vessels. These bands were most dense at the hilus of the lung and radiated from it to the pleura. They were connected with the thickened pleura at the depressions. This tissue was hard and tough, was almost devoid of air, and of a grayish, slaty color. The large bronchi were slightly dilated. In the thickened tissue there were several caseous nodules surrounded by firm capsules of transparent connective tissue.

The left lung showed lesions of the same character. More than one-half of the entire lung was consolidated, both from an interstitial process along the bronchi and a mottled-red infiltration accompanying this. There were several small, hard nodules beneath the pleura. These were surrounded by zones of fibrous tissue from which bands were given off, which penetrated the lung for some distance, but were not connected with the bronchi. Pus could be squeezed from all the bronchi in the consolidated lung. Microscopic examination of the fibrous tissue along the bronchi showed a rather

[1] Reported by Councilman, *Johns Hopkins Hospital Bulletin*, 1891, vol. ii.

loose connective tissue containing few cells. The bronchi showed a growth of fibrous tissue into the lumina. Some were entirely obliterated, their place being marked by the remains of the muscular tissue. The lung adjoining these fibrous portions was in a state of acute inflammation. The alveoli were filled with fibrin and leukocytes. The walls of the alveoli were thickened and infiltrated with cells.

There can be no question, of course, that the condition in this lung was the result of syphilis, and it represents the most common form. In another case the condition was different—not a fibrous phthisis with emphysema, but an extensive gummatous caseation with softening and cavity formation—a true syphilitic phthisis. A colored man,[1] aged twenty-seven, was admitted to the Johns Hopkins Hospital with hæmoptysis. For more than a year he had had cough and shortness of breath and he was regarded at the out-patient department as tuberculous. He had weakness and wasting of the left arm. The physical signs were at the apex of the left lung with impairment of resonance and numerous rales, and there were signs of extensive disease of the right lower lobe. He died suddenly of hemorrhage from the lungs. The case was regarded as one of pulmonary tuberculosis, although no bacilli had been found in the sputum. At the postmortem the apex of the left lung felt firm and there were a few scattered nodules on its surface. On section, just below the apex, there was a caseous mass surrounded by a scar-like tissue. The right lower lobe was almost entirely solid with caseous masses, separated by strands of connective tissue. In the middle there was a cavity (not bronchiectatic) of 3.5 cm. in diameter, filled with blood, which opened directly into a bronchus, and which had eroded into a branch of the pulmonary artery. This case shows the existence of a progressive destructive disease, a true syphilitic phthisis. No tubercles or tubercle bacilli were found. An important point mentioned by Remsen is the fact that there was cavity formation due directly to the disintegration of caseated tissue. Councilman and other writers on the subject have expressed the belief that most of the cavities in syphilitic phthisis are bronchiectatic.

The *symptoms* of pulmonary syphilis are very uncertain. Practically they are those of tuberculosis, but with the physical signs more commonly at the root of the lung and toward the base. The clinical features are often those of chronic bronchiectasis or fibroid phthisis. In the cases with tracheal or bronchial stenosis dyspnœa is a special feature. Hæmoptysis may occur, as in the case here described. There may be no fever, but when softening has occurred or when there are large bronchiectatic cavities the temperature may be of the hectic type. J. K. Fowler lays down the following conditions necessary to determine the syphilitic nature of a case with progressive disease of the lung: "(1) The cases must be complete, that is, the symptoms observed during life must be considered in connection with the lesions described in postmortem examination; (2) the evidence of syphilitic infection must be undoubted; (3) repeated examination of the sputum must have been made and tubercle bacilli have been invariably absent and the absence of tubercle from the lungs (as the cause of the lesions) must be proven by postmortem examination; (4) syphilitic lesions about the nature of which there can be no doubt must be found in other organs."

[1] Reported by Remsen, *Johns Hopkins Hospital Bulletin*, vol. xix.

*The relations of syphilis and tuberculosis* are thus described by the same writer with admirable clearness. "(1) Tubercle usually affects the apex of the lung and subsequently the apex of the lower lobe and tends to progress in a certain route. The primary lesion of syphilis is often about the root and central part of the lung. The disease follows no definite line of march and gummata may be found in any position. (2) Both tuberculosis and gumma may undergo either necrosis and caseation of fibrous transformation, but with caseous tubercle the tendency toward softening and cavity formation is the rule, whereas a caseous gumma very rarely breaks down. (3) The progressive destruction of the lung by a process of disintegration leading to a gradual increase in size of a cavity, a change so commonly observed in tuberculous disease, is rarely if ever observed in syphilis, except as a secondary result of stenosis of one of the main bronchi. (4) In nearly all cases of advanced destruction of the lung occurring in the subjects of syphilis, stenosis either of the trachea or of one of the main bronchi is present, whereas this lesion is very rare indeed in tuberculosis. (5) The cavities found in cases of pulmonary syphilis are usually bronchiectatic, but not invariably so; whereas in tuberculosis they are commonly due to progressive destruction of the lung, but may be bronchiectatic. (6) The tendency to the formation of pulmonary aneurisms, which is so marked a feature in tuberculosis, is rarely observed in pulmonary syphilis. (7) Pulmonary lesions in tuberculosis are very common, whereas in syphilis they are extremely rare" (Fowler).

II. **Syphilis of the Alimentary Canal and Abdominal Organs.**—1. SALIVARY GLANDS AND PANCREAS.—Swelling of the salivary glands occurs in the secondary stage and it may be well developed before mercurials have been given. In two instances in students, the condition was at first thought to be ordinary mumps. Chronic bilateral parotitis with enlargement, a not very uncommon condition in hospital patients, is probably not connected with syphilis. Gummata of the salivary glands have been described, sometimes with ulceration.

The *pancreas* is rarely attacked and Herxheimer gives only three cases from the literature, all with gummata.

2. ŒSOPHAGUS.—In a few rare instances ulceration of this part has been seen, usually as an extension from the pharynx. Stenosis as a sequel of the ulceration has been described by Virchow and others.

3. STOMACH.—Great difference of opinion exists as to the frequency of syphilitic lesions of this organ. The clinical evidence is by no means trustworthy, as there are men who see a specific gastritis in every disturbance of digestion in a syphilitic patient. The best evidence of its rarity is the fact that in Chiari's 243 postmortems upon syphilitic patients there were only 2 with definite stomach lesions due to the disease.

Flexner, in describing a very characteristic example in 1898, could only find 14 trustworthy cases in the literature. Of these 9 were acquired and 5 were of the inherited form.

There are three types of lesions: (*a*) *Diffuse syphilitic gastritis*, which was present in a syphilitic negro (examined by Flexner) who had gummata on the frontal bone, in the liver, and in one testis. Hemmeter gives a very good picture of the diffuse gastritis present in the case in the form of a small, round-celled infiltration.

(*b*) *Syphilitic Ulcer.*—The majority of clinical cases reported have presented the symptoms of ulcer in connection with the history of syphilis. Fenwick

very correctly concludes that in fully one-half of the cases in which the two diseases co-exist in the same patient there is no direct relationship between them. The chief evidence of the specific character of the lesions is the ready response to antisyphilitic treatment, perhaps after prolonged trial of other measures. As there seem to be no distinctive features of the syphilitic ulcer, this point has been especially insisted upon, particularly by Stockton and by Einhorn, who have reported interesting cases. Fenwick concludes that "these cases chiefly differ from the simple variety of the disease in three particulars, the first of which is the extreme severity of the pain and vomiting, the second the infrequency of hemorrhage, and the third their obstinacy to ordinary treatment and their great tendency to relapse." We do not, however, think it possible to draw a clear distinction between simple and syphilitic ulcer, although it is well to bear in mind the undoubted existence and the possible frequency of the latter condition.

Naturally, the experience of anyone with syphilitic ulcer is very limited. Of one or two instances with well-marked symptoms of ulcer of the stomach in connection with other syphilitic lesions, it was impossible to be certain of the specific character of the stomach trouble. Perhaps the most definite case was one which was referred from Montreal and which was subsequently reported by Lafleur.[1] The patient, aged thirty-seven, had had syphilis ten years before. For about six months he had had very severe stomach symptoms, frequent vomiting with very little actual pain. He had lost thirty pounds in weight. There was no hydrochloric acid in the gastric juice. Although his color was good he had become very thin and weak. The stomach was moderately dilated, with visible peristalsis after inflation, and there was a great difference in the consistency of the stomach wall as the waves of peristalsis passed. An exploratory operation by Dr. Armstrong, of Montreal, showed perigastric adhesions and an extensive area of ulceration fully four inches in extent along the anterior wall. The edges were undermined, the surface smooth and almost bloodless. Dr. Lafleur suggested the specific nature of the ulcer and the patient was given antisyphilitic treatment. He gained rapidly in weight, there was no recurrence of the vomiting, and he has remained well ever since. This seems to have been a very characteristic case. While, of course, it is possible that it was only a simple ulcer of unusual dimensions, there were special features about the lesion. The soft, overhanging edges and the dry and bloodless base, and the long, tag-like adhesions on the external surface presented a picture almost indentical with that described and figured by Flexner. A point of some moment is the histological character, which was very similar to that found in Flexner's case.

This case, which has been reported fully by Dr. Flexner,[2] was in the Johns Hopkins Hospital on several occasions. He was first admitted February 14, 1893, when he was forty-eight years of age. He had had a primary sore ten years before. In January, 1890, he had irregular fever, with pains in the abdomen. His evening temperature was sometimes as high as 103.5°. He gradually improved. In July, 1902, he had diarrhœa and the legs and abdomen became swollen. The dropsy did not disappear until November. He had lost nearly eighty pounds in the past two years. There was no jaundice. The liver could not be felt. The spleen was enlarged. We

[1] *Transactions of the Association of American Physicians*, vol. xviii.
[2] *Ibid.*, vol. xiii.

regarded the case as one of ordinary cirrhosis of the liver. He returned on March 4, 1894; in the interval the abdomen had been tapped forty times. The spleen was greatly enlarged. On November 30, 1894, he returned again. He had been tapped up to date sixty-five times. He had been using potassium iodide freely and had been gaining in weight. Then one day he had a sudden pain in the abdomen, signs of acute perforation, and he died of peritonitis. The liver was reduced in size, particularly the left lobe, which was represented by a shrunken mass formed by the confluence of several gummata. The mass formed a fibrous tumor 11 by 5 cm. It extended into the right lobe. The spleen was enlarged and hard, measuring 12 by 17 cm. In the greater curvature of the stomach was an open ulcer 5 by 5 cm., with puckered, overhanging margins, and in the centre a perforation.

(*c*) *Gumma* of the stomach is exceedingly rare. Of the 14 cases collected by Flexner 5 or 6 had positive nodular gummata, the largest formed a flat tumor 8 cm. in extent, with slight ulceration on the surface. In no instance has the diagnosis of a gumma during life been confirmed at autopsy.

In connection with syphilis of the stomach there are two conditions in which tumor may be present. At the pylorus, or in its neighborhood, there may be nodular thickening and it is quite possible that in certain of the cases in which gastric tumors have disappeared entirely, the lesion has been specific. Several of the suggestive cases recorded by Einhorn are of this nature. Following the scar of the syphilitic ulcer near the pylorus, the orifice may be narrowed, with the result of great dilatation of the stomach. In a more important group of cases the tumor believed to be in the stomach, is in reality a gumma of the left lobe of the liver adherent to the anterior wall. We have seen two or three patients with suspected carcinoma of the stomach with epigastric tumor in whom the condition has apparently been caused by a gumma on the left lobe of the liver, simulating very closely carcinoma. Mayo Robson and Moynihan, in Plate XXX of the second edition of *Diseases of the Stomach* show a stomach the cardiac orifice of which was obstructed by a gumma, which also involved the adjoining portion of the liver.

(4) INTESTINE.—In the small bowel, which is less frequently involved, there may be enteritis, gummata, ulceration with consecutive cicatrization and narrowing. The so-called syphilitic *enteritis* offers nothing peculiar. There is swelling of the lymphatic follicles, sometimes with small ulcers. In long-standing cases of tertiary syphilis with chronic diarrhœa, amyloid degeneration of the mucous membrane is not uncommon, sometimes with definite ulceration.

*Ulcers.*—Apart from the follicular ulcers in the enteritis of syphilis there may be quite extensive loss of substance due to the breaking down of gummata. The ulcers involve the lower part of the jejunum and the ileum. In a few cases perforation has taken place. Healing of the ulcers may lead to cicatricial contraction with stenosis, and there are cases on record in which in several places the calibre of the jejunum and ileum was narrowed. Appendicitis has been attributed to syphilis, but there is no evidence that persons with this disease are more frequently attacked than others.

5. RECTUM.—The special liability of this part to the disease is doubtless the result of a direct infection by the secretion, either from the vulva or from condylomata. In a few instances the ulceration follows the breaking down of gummata. The loss of substance, often very extensive, is usually circular, and in healing leads to marked stenosis. The condition is very much more

frequent in women than in men. The stage of ulceration may be quite latent, and the patient is not infrequently first seen when narrowing has already taken place. The wall of the bowel is greatly thickened, the muscular coat much hypertrophied, the mucosa roughened, or actually ulcerated, and the lumen narrowed so as to admit the little finger with difficulty. Periproctitis is a common sequence, and in women the pelvic peritoneum may be greatly thickened. The ulcers may perforate with the formation of a pelvic abscess or a rectovaginal fistula. The diagnosis rarely offers any difficulty, although the syphilitic rectum has been excised for cancer. The greater frequency in women, the marked thickening of the walls with narrowing of the lumen, and the absence of definite marginal growths about the ulcers are important points. The presence of other lesions, the fact of recurring miscarriages in a woman or the presence of syphilitic lesions in the husband may help in the diagnosis. A remarkable form of syphilitic tumor of the pelvis has been described in which the connective tissue is chiefly involved, forming a dense mass in which the organs are embedded. Herxheimer cites 4 cases from the literature and reports 1 of his own. In one instance the pelvis was occupied by a tumor the size of two fists, situated between the bladder and the rectum, and which very naturally during life was thought to be cancer. The mucosa of the rectum may be intact.

6. SPLEEN.—In the early stages of the disease enlargement of the organ may usually be determined, and Moxon has described an acute syphilitic splenitis.

*Gummata* are common, particularly in cases where the liver is involved. The substance of the organ may be thickly set with growths varying in size from a walnut to a large orange. Wilks'[1] description and figures are excellent, and he was one of the first to recognize the true nature of these bodies. They are very rare in the congenital form (Still).

*Gummous Cicatrices.*—More frequently the organ is enlarged, the capsule thickened, the surface indented and scarred and fissured, even divided into four or five sections; the liver and spleen may look very much alike. The greatly enlarged and irregular organ may present a remarkable degree of mobility.

*Amyloid Spleen.*—In long-standing cases, particularly those with disease of the bone and of the rectum, amyloid change is common either as a diffuse process with enlargement of the organ or limited to the Malpighian bodies, the so-called sago spleen. And, lastly, in certain cases of syphilis with enlargement of the liver and spleen the degree of leukocytosis is such that leukæmia is suspected. In a case of congenital syphilis with an extraordinarily fissured liver, the spleen weighed more than 1500 grams. It was the most prominent feature in the distended abdomen. There was great increase of the leukocytes and the case was regarded as one of leukæmia until the postmortem showed the existence of congenital syphilis.

7. LIVER.—Whether the liver was attacked by syphilis was much disputed by the older writers, some of whom maintained that it was, while others particularly Morgagni, thought that this organ was exempt. Our accurate knowledge dates from the studies of Ricord, Rayer, Dittrich, Wilks, and Virchow. The recent literature is very fully given by Herxheimer in Lubarsch and Ostertag's *Ergebnisse*, Jahrg. xi, and the whole subject is dis-

[1] *Transactions of the Pathological Society of London*, 1871.

cussed at great length in a masterly way in Rolleston's work on *Diseases of the Liver.*

*Incidence.*—It is difficult to determine the frequency with which the liver is involved. Once attention has been called to the subject and the special features have been recognized the cases are found to be not so very uncommon; in the records at the Johns Hopkins Hospital during a period of eighteen years there were 30 cases diagnosed as such, while in the postmortem room among 2500 autopsies there were 40 cases showing gummata or syphilitic cicatrices (20 of each) and 15 additional cases regarded as syphilitic cirrhosis. Among 5088 postmortems analyzed by Flexner, interstitial changes were found in 42, gummata in 22, perihepatitis in 16, amyloid degeneration in 70, and syphilitic scars in 38. In the postmortem records of St. George's Hospital for a period of forty-two years, in 11,629 autopsies, there were only 37 cases of gummata and in 27 other cases cicatrices alone were found (J. L. Allen). These figures give no idea of the actual frequency of the lesions. Statistics of this sort are not of much value unless the postmortems have been made with special attention to their collection. The story of the incidence of tuberculous lesions has impressed this truth upon us. The incidence in congenital syphilis is very much higher and has been given at from 40 to 70 per cent. of cases of infants born prematurely or dying shortly after birth.

*Morbid Anatomy.*—The lesions may best be described in four groups: (1) *Diffuse interstitial hepatitis.* This is common in the congenital form, in which the liver is usually enlarged, very firm, with a peculiar color, described as grayish-yellow or having more the appearance of flint—the *foie silex* (Gubler). The cut surface may be uniform, and frequently miliary gummata are to be seen. The process may be much more advanced in some parts of the liver than in others, and there may be large areas of fibrosis. Microscopically in the early stages there is diffuse small-celled infiltration and the gradual production of a cirrhosis which may be monolobular or multilobular; and in nearly all instances there is extensive fibrosis within the lobules themselves. (2) *Gummata.* These characteristic structures consist of large, opaque, white tumors, usually firm and solid, the cut surface resembling a section of potato and much denser and harder than the ordinary cheesy matter of tuberculosis. It is not surprising that the older writers thought these tumors to be cancerous. Surrounding the gumma is a definite zone or capsule of connective tissue, and outside that a zone of translucent tissue representing the small-celled infiltration of the advancing syphilitic process. In fresh gummata of all sizes the three zones may be recognized. In old ones the translucent zone is absent. The tumors vary in size from small nodules of from 2 to 4 mm. in diameter to huge tumors the size of two fists. They may be solitary, more frequently there are from 3 to 4, or in some instances 12 or more. Gummata undergo retrogressive changes. Just as the massive subcutaneous, muscular, or periosteal tumors, those of the liver may disappear completely, leaving only a fibrous scar. It would seem scarcely possible that a tumor on the surface of the liver feeling as big as the two fists could disappear, yet we see large gummata of a testis or multiple subcutaneous tumors, even of maximum size, melt away under appropriate treatment. Softening may occur in the centre of a large gumma, either from the breaking down of the necrotic tissue or occasionally from septic infection. No change may occur in the consistency of a large gumma

while it is undergoing even rapid absorbtion. Calcification may occur, and the rare instances of diffuse calcification in wide areas in the liver have probably been of this character. (3) *The scarred and the botryoid liver.* There may be (*a*) small, puckered depressions on the surface, with perihepatitis, but with very little actual deformity of the organ. These small scars may be central as well as peripheral. There may be nothing in the liver itself to show that these are the remains of healed gummata, but in other cases specific lesions may be present elsewhere or in the other parts of the organ itself. (*b*) One or both lobes may be divided by bands of fibrous tissue, radiating irregularly from the hilus or following the portal canals. The bands may be from 5 to 10 mm. or more in diameter and the lobes may be greatly puckered and deformed. Sometimes there are gummata associated with these cicatrices. In extreme cases the whole surface of the organ is lobulated, and to this condition the term "botryoid" has been given. In a still more extreme form large sections of the liver may be completely isolated, or the organ may be made up of three or four sections united by flat bands of connective tissue. The liver substance itself may look natural, or it may show slight cirrhotic changes. Occasionally it is amyloid. (*c*) Amyloid change may co-exist with gummata, or it may occur independently in long-standing tertiary lesions.

*Symptoms.—Congenital.*—In the majority of cases the infants do not live. In children under two years the luetic appearance, together with an enlarged abdomen due to an increased size of the liver and the spleen, are the most usual manifestations. The enlargement of the liver is uniform and may be very great, reaching below the level of the navel. Tumors are very rarely felt, but the organ is firm; very often the edge may be pressed readily with the finger, or through a thin-walled abdomen the shadow of the edge of the organ may be seen to descend with inspiration. As Gee pointed out years ago, enlargement of the spleen is almost constant in syphilitic children. Jaundice is not very common and when it occurs is early. Ascites is rare.

In general practice a much more important group of cases is the syphilitic hepatitis which occurs as a late manifestation. The attention of the senior author was called to this form by a very remarkable case in the practice of Palmer Howard, of Montreal: A boy aged ten years had for several months obscure abdominal trouble with enlargement of the liver, slight jaundice, ascites, enlargement of the spleen. Finally, definite, irregular nodules were felt on the liver, whether tuberculous or malignant we were in doubt. One day his father was discovered to have a very characteristic palmar psoriasis. He confessed to having had a syphilitic infection as a young man. This gave us the diagnosis, and after months of serious illness the boy recovered promptly and is still alive, now some thirty years after the attack. Since that date a number of very interesting cases have been seen, several of which have been reported.[1]

J. G. Forbes[2] has analyzed 132 cases of late congenital syphilis and in 34 per cent. the liver was involved, coming next to the bones (39 per cent.), as the seat of disease. The age incidence is worth noting—the first decade 26.5 per cent., second decade 57.5 per cent., third decade 12.3 per cent., fourth decade 3.7 per cent. The clinical features are often very characteristic.

[1] *Lectures on Abdominal Tumors*, 1895.
[2] *St. Bartholomew's Hospital Reports*, vol. xxxviii, p. 37.

The facies, the interstitial keratitis, the rhagades, the Hutchinsonian teeth, the dwarfed stature, sometimes infantilism, or the clubbed fingers—one or other of these points may clinch the diagnosis in an obscure abdominal case with symptoms pointing toward the liver. The symptoms do not differ materially from those of adult syphilis of the liver and there may be the three groups of cases: the enlarged, irregular liver, with pain due to the perihepatitis; fever, and an obscure abdominal condition the nature of which is entirely overlooked unless some clue is furnished. A boy at present in attendance at the Radcliffe Infirmary has a small, irregular liver, a big spleen, infantilism, and an increased pigmentation of his skin. Three or four years previously he was in the Westminster Hospital for a very obscure disease characterized by enlargement of the liver, and slight jaundice, with fever. The second group of cases, those with tumor on the surface of the right or left lobe, present no special features, and lastly there may be a final stage of the syphilitic hepatitis in which there is portal constriction, enlarged spleen, and ascites. Under the section on syphilis of the spleen the fact is noted that in certain of those cases there may be marked leukocytosis and a clinical picture resembling leukæmia.

*Clinical Features in the Adult.*—The manifestations are most protean and the cases may be grouped, as Rolleston suggests, into (1) those with *features of hypertrophic cirrhosis.* A man with a history of a primary sore has pains in the region of the liver, slight jaundice, and on examination the organ is found to be enlarged, reaching to the navel or even a hand breadth below it. It is usually tender and possibly a little irregular, but in some cases it may be quite smooth. One of Stockton's cases, seen with him, was of this character, and it was remarkable how the really enormous liver gradually reduced in size and the patient recovered. (2) The cases resembling ordinary *atrophic cirrhosis with recurring ascites,* enlarged spleen, and all the ordinary features of hepatic dropsy. The portal obstruction may be due to direct pressure of large gummata on the main branches, or the stenosis may follow cicatrization. Such a case as the one the abstract of which is given under syphilitic ulcer of the stomach had a very characteristic picture: there was recurring ascites for two or more years, with great loss in weight, and the postmortem showed a contracted, gummatous tumor which had almost obliterated the left lobe and compressed the portal vein at the hilus. In the *Lectures on Abdominal Tumors* the report of another case of similar character is given; this was a woman who had been very frequently tapped before admission, and in whom the diagnosis of syphilitic hepatitis was made by the accidental examination of her shins. She recovered promptly and some years afterward died suddenly just prior to her confinement. The liver showed the old healed gummata. Undoubtedly many of the cases of cured alcoholic cirrhosis are of this nature. It is sometimes impossible to get positive evidence of syphilis, but in a patient who has been going from bad to worse and has had to be tapped repeatedly, if recovery occurs promptly under syphilitic treatment, it is fairly good evidence as to the nature of the disease. (3) *Hepatic Tumors.* The syphiloma on the surface of the right or left lobe may form a visible or palpable tumor, or there may be multiple nodules on the surface of the organ. Such cases are not very common, and personal experience coincides very closely with that of Einhorn. Several very characteristic cases are reported in the *Lectures on Abdominal Tumors.* There may be a small, solid nodule easily felt attached to the

right or to the left lobe. It is painless, and may remain unchanged for months. The nature of the case may only be determined by the development of a gumma elsewhere, or a tumor may arise in the epigastrium in a patient with slight fever, anæmia, loss in weight, and the diagnosis of gastric carcinoma is made; or there may be a huge tumor the size of the two fists upon the surface of a greatly enlarged liver and the volume of the tumor may throw the practitioner off the scent. In 1896 we had a remarkable illustration in a soldier who had a large, prominent tumor between the ensiform cartilage and the navel. It had grown gradually since September, 1893. Much discussion had taken place as to its nature. He had been in many hospitals and the tumor had been tapped several times. He had a well-defined history of syphilis, and giving him the benefit of the doubt, he was placed upon large doses of iodide. It is scarcely possible to believe the change which occurred. He was shown repeatedly at the out-patient clinic, the pains lessened, the tumor slowly disappeared, and finally on November 11th, which was ten months from the date of his first visit, the tumor had almost entirely disappeared. The liver was reduced in volume. The edge could be felt 4 inches below the ensiform cartilage, irregular and rounded. On February 25th, a little more than a year from his first appearance, he returned, having gained fifty pounds in weight. He was so stout that it was impossible to make an examination of his liver. In several of the cases the diagnosis of malignant disease had been made. An important point in the diagnosis of these cases is the almost invariable association of enlargement of the spleen. Of course, there is nothing in the tumor itself which is of help in the differentiation from malignant disease. The syphilitic liver may be just as large and irregular as the cancerous, but there is rarely the rapidity of growth or the cachexia. (4) *Amyloid Liver.* In long-standing cases with necrosis of bones and in extensive gummatous disease the liver may be greatly enlarged with amyloid degeneration. The organ may be smooth and uniform, or there may be nodular irregularities due to gummata or other cicatrices. The spleen is usually greatly enlarged. Albuminuria is usually present with dropsy, and the general features of the cases are renal. Rolleston gives a case in which the liver weighed eight pounds and ten ounces. (5) *Cases Resembling Abscess.* The enlargement, the tenderness, the fever, and the slight jaundice, not unnaturally lead to the suspicion of suppuration, and if in addition to these there is a prominent tumor the suspicion becomes almost a certainty. The liver has been aspirated. Sometimes a gumma becomes secondarily infected and softens and forms an abscess; (6) and lastly, there are instances in which the great enlargement of the spleen and the diminished area of the liver suggest a primary blood disease, a *splenic anæmia*, or, if the liver is reduced in size, Banti's disease. Coupland has reported a case in which the large spleen was removed, but the woman died from hæmatemesis. The liver was found to be syphilitic.

III. **Renal Syphilis.**—Morgagni was the first to recognize that the kidneys were involved in the disease. Our modern knowledge dates from the studies of Rayer. The literature is very fully given by Herxheimer.

The most important renal complication is acute nephritis, a not at all uncommon event, but one to which comparatively little attention has been paid. The French writers have for long recognized its importance, and Lafleur, of Montreal, brought the subject before the Association of American Physicians in 1896. Early in the nineteenth century the presence of albumin

in the urine of syphilitics was noted by Wells, Blackall, and others, but it was attributed to the use of mercurials. Rayer pointed out that it occurred as a result of the disease itself, and this view has been amply sustained. There may be simply slight and transient albuminuria, just such as occurs in the initial stages of any acute infection. In other instances the symptoms of nephritis become manifest within from two to four months of the initial lesion. In the majority of the cases it occurs with the cutaneous outbreak. The nephritis of the later period of the disease is of a different character, and depends upon amyloid change. The pathological changes described by Cornil resemble very closely those of scarlatinal nephritis.

The symptoms are those of acute or subacute nephritis. There is rarely any fever. The onset is insidious, usually without any pain in the back, and œdema is the first symptom noticed. It may be confined to the face and legs, or it may become general. The urine is diminished in quantity, smoky, contains blood, tube casts, and much albumin. After persisting for five or six weeks the albuminuria lessens, the dropsy disappears, and the patient makes a good recovery. A few cases have been reported in which a fatal event has followed in from fourteen to twenty-one days. Chronic nephritis is an occasional sequence. The nephritis may also occur in hereditary syphilis. Chronic interstitial nephritis is met with in old syphilitics, and is, as a rule, the sequence of arterial changes. It is more commonly a patchy atrophy of areas of the cortex than a uniform general involvement of the organ.

*Amyloid disease*, which is so common as a late manifestation of syphilis, presents no special features and requires here no detailed description.

*Gummata.*—The kidney is not often affected; when present the tumors are small, multiple, and rarely cause symptoms; even when a dozen or more pea-sized tumors are present there may be nothing to indicate their existence. In a few cases the kidney is the seat of enormous gummous tumors. Boldby[1] has reported the case of a woman, aged forty, with swelling in the right renal region. The kidney was enlarged, hard, and easily movable, and evidently the seat of a tumor of considerable size. A new-growth was diagnosed and the organ was excised. It weighed seventeen ounces and the surface was nodular on section. It cut like fibrous tissue and the surface presented an appearance exactly like that of a gummatous testis. All trace of renal tissue had disappeared. The microscopic examination showed typical, small-celled infiltration and caseous degeneration. The patient recovered rapidly, but, as Boldby remarked, for the future it must be borne in mind that a renal tumor of considerable size may be caused by syphilis, and it is probable that antisyphilitic treatment would have obviated the necessity for operation. Here may be mentioned the remarkable association of diabetes insipidus and cerebral syphilis which is present in a considerable proportion of all cases. Of the 9 cases reported by Futcher, 5 had this association.

IV. **Syphilis of the Circulatory System.**—BLOODVESSELS.—Upon no system does the virus of the disease fall with greater intensity in all stages than upon the bloodvessels. It is safe to say that through the arteries syphilis kills more than through any other channel. Cerebrospinal lues is largely a matter of arterial disease. The gummata often originate in or about the bloodvessels. The late arteriosclerotic changes leading to fibrosis are very

[1] *Pathological Society Transactions*, vol. xlviii, p. 128.

often due to the toxins of the disease; but, above all, the association of aneurism with syphilis gives a place of first importance to its vascular aspects. Those acute old writers, Ambrose Paré and Morgagni, appreciated very clearly the frequency of arterial disease in syphilitic patients. In his classical chapter on aneurism there is scarcely a case in which Morgagni does not refer to the presence of syphilis. The recent very extensive literature is given in the papers of Benda and Chiari.[1]

*Gummata of Arteries.*—The larger vessels are rarely the seat of distinct gummous tumors. Three changes are met with in the smaller bloodvessels:

1. *The Nodular Periarteritis.*—In this form many of the branches of the circle of Willis present nodular tumors, which may be from 3 to 5 mm. in diameter, oval in shape, firm and hard, often associated with gummous meningitis, or with numerous large gummata. The tumors are larger and firmer than in the nodular arteritis of tuberculosis. On section the nodular process seems to be almost entirely in the adventitia, sometimes with subintimal proliferation and with great narrowing of the lumen.

2. *Acute Gummatous Endarteritis.*—This, too, is most frequently seen in the cerebral arteries, but it has been described in the larger branches, and it is quite possible that the acute perforating ulcer of the aorta is of this nature. The lesion consists of a localized gummatous infiltration of the subintimal tissue, with softening and erosion leading to the production of aneurism or to perforation. This may occur quite early in the disease.

3. *Obliterative Endarteritis.*—This is seen most commonly in arteries of medium or small caliber. It may be limited to one or two vessels, as to one of the coronaries in which it is not at all infrequent, or to a posterior tibial. The endarteritis leads to a gradual narrowing and a final obliteration of the lumen. There is nothing specific in the process itself. So far as known, the spirochæte have not been found, but it is a lesion met with in comparatively young persons with syphilis, which may be associated with gummatous lesions. An identical endarteritis may occur as a senile change or as a result of toxic agents. For the histological changes the reader is referred to text-books on pathology.

*Syphilitic Arteritis.*—This is seen chiefly in the large branches, particularly the aorta, and is one of the most important of all the lesions of syphilis. It has nothing to do with the ordinary atheroma. While it may occur in persons above the middle period of life, it is most commonly seen in those under forty who have been the subjects of syphilis. It presents several special features: (*a*) The process may be limited to a small section of the aorta, an inch or so, for example, at the root, or a patch extending for a couple of inches in extent anywhere in its course. The intima in the rest of the extent may be quite smooth. The parts of the aorta most frequently involved are the root, and the lower part of the thoracic and lower part of the abdominal aorta. The appearance differs very markedly from that seen in ordinary atheroma, particularly in the absence of calcification and of fatty degeneration and of areas of atheromatous softening. While in the early stage the intima may be smooth and the mesarteritis entirely microscopic, in the later stages the intima presents the appearance of what Marchand has called the scarring sclerosis. The intima looks wrinkled with linear depressions or little

[1] *Verhandlung. der Deutsch. Path. Gesellschaft,* 1903, and Lubarsch und Ostertag, *Ergebnisse,* 1904 and 1906.

pockets, or there may be puckerings or scar-like fissures, sometimes arranged in a radial manner. The bottom of some of these depressions has a bluish tint, and held up to the light the vessel here looks translucent. (*b*) Microscopically the changes are very remarkable and consist in (1) extensive degeneration of the elastic fibers of the media, which is shown very well with the Weigert stain; (2) areas of small-celled infiltration, sometimes focal, sometimes linear. These two features of destruction of the elastic and of the muscular elements, with the widespread, small-celled infiltration often localized sharply in a media otherwise healthy, is the most characteristic microscopic change. (3) The changes in the adventitia are often even more marked than in the media and consist of areas of round-celled infiltration which may be quite extensive and look like microscopic gummata. They frequently surround the arteries and they extend in linear form between the boundaries of the media and adventitia, or they may be traced in direct continuity with similar linear collections in the media. With this there is a marked obliterative endarteritis and endophlebitis of the vasa vasorum: (4) In the larger areas of small-celled infiltration giant cells are found and even patches of necrosis; and lastly, and this is an all-important point, Schmoll, Reuter, and others have found the spirochæte in these lesions.

It is quite possible, of course, that other acute infections may lead to similar changes in the bloodvessels, and much discussion has taken place as to the specificity of those here described, but the evidence points strongly to the fact that syphilis is, at any rate, one of the most potent factors in the production of this form of arteritis, and the discovery of the spirochæte seems to clinch the view which has been so well maintained by Chiari and others.

*The Relation of Syphilis and Aneurism.*—Morgagni seemed to be fully aware of an important relation between these two diseases. Welch, in 1876, called attention to the frequency of aneurism in soldiers and thought that at least 50 per cent. of the cases were associated with syphilis. Since then in the collections of statistics the percentage has ranged from 20 to 80. The same difficulty has occurred here as with locomotor ataxia. The more carefully the cases are looked into, the more accurately they are studied, the larger will be found to be the percentage of cases with the history of lues. One feature which has impressed the writers on the subject is that the age incidence of aneurism and of ordinary atheroma is different. In a large proportion the patients are in the third and fourth decade. The studies of Chiari, Benda, and others show that the type of mesaortitis here described is almost constantly present in cases of aortic aneurism. The recent experimental production of aneurism by the administration of adrenalin lends support to the view. The necrosis and degeneration is produced in the media, over which there may be a perfectly smooth intima; in places this may crack, and through the narrow fissure the blood passes and gradually a small aneurismal sac is produced. This is probably the sequence of events in the majority of cases of aneurism in man. The aortic wall is weakened in its most important coat by the destruction of elastic and muscular fibers, and during a sudden exertion, or spontaneously, the intima is split, with the formation of, first, a small aneurism which gradually increases in size. Of course, this does not exclude the origin of aneurism in a small proportion of cases from ordinary atheroma.

SYPHILIS OF THE HEART.—The cardiac lesions of syphilis may be considered under the headings of endocarditis, fibrous myocarditis, and gummata.

*Endocarditis.*—Whether there is an acute endocarditis caused directly by the spirochæte is not yet settled. Taneff recognized a verrucose syphilitic endocarditis as a very rare form. Much more commonly it is a sclerotic form which may be either mural or valvular. The former is met with as thickened patches of the endocardium, chiefly of the ventricles, sometimes in direct connection with gummata in the myocardium. It is impossible to determine the specific character of an ordinary sclerotic valvulitis in a syphilitic subject. The cases most likely to be of this nature are those in which the valves are implicated directly in scarring of the mural endocarditis or in a patch of fibrous myocarditis. There is a very important group of cases in young syphilitic subjects who come under observation with angina pectoris, and who present signs of aortic insufficiency. The semilunar valves are involved with the root of the aorta in a specific mesarteritis and peri-arteritis. A strong evidence in favor of the luetic nature is the complete relief afforded by antisyphilitic treatment, the aortic insufficiency, of course, remaining.

*Fibrous Myocarditis.*—This is seen most frequently in the left ventricle and near the apex. In many cases it follows directly upon endarteritis of the descending branch of the anterior coronary artery. Unless gummata are present, or there have been well-marked signs of syphilis, it may not be possible to determine the specific character of the lesion. When extensive, it may lead to aneurism of the heart. In other instances the scarring in the myocardium is due to healing of small gummata. Widespread areas of fibrous myocarditis in syphilitic patients are most frequently the result of arterial disease.

*Gumma of the Heart.*—Stockmann, who has written a monograph on the subject (Bergmann, 1904), was able to collect 76 cases from the literature. The gummata may be small and multiple, or there may be a tumor as large as a walnut. The appearances are those of gummata in other parts.

The *symptoms* of syphilis of the heart are indefinite. Sudden death is not uncommon. Of the 6 cases reported by Herringham all but 1 were brought into the hospital either dead or dying. Symptoms of dilatation are perhaps the most common. Attention has been directed particularly to two forms—the syphilitic variety of Stokes-Adams disease, in which there is either a gumma at the top of the septum, as reported in one of Keith's cases, or it may follow a syphilitic endo-arteritis. Two of our patients were syphilitic. One of the cases reported by Erlanger had bradycardia and epileptiform seizure for a year or more and recovered completely under specific treatment. The other group is the aortic insufficiency in young subjects, which may come on with attacks of angina pectoris. They also may be greatly relieved by appropriate treatment.

*Syphilis of the central nervous system*, one of the most interesting and important forms of the disease both on the clinical and pathological sides, will be discussed under Diseases of the Nervous System.

**The Tertiary Cutaneous Syphilides.**—The tertiary syphilodermata are rarer than those of the secondary stage and vary less in type. They tend to become grouped or localized.

(*a*) The *tuberculous syphiloderm* is one of the earliest of the tertiary manifestations. The lesions appear first as small, brownish-red nodules, which gradually reach a considerable size and then undergo central disintegration. At the same time the lesion advances at the periphery by infiltration, and since this takes place more or less irregularly the ordinary picture is that of disintegrated tubercles with advancing crescentic walls of infiltration inter-

spersed with superficial scars. The coalescence of adjacent nodules gives rise to the serpiginous and circinate syphiloderm. The eruption is usually confined to one part of the body, the forehead, the nape of the neck, the upper part of the back, and the scrotum being the favorite sites. The differentiation from lupus vulgaris and lupus erythematosus may be difficult. On the palms and soles the tuberculous syphilide is a common manifestation of the disease. The lesions are often circinate and are accompanied by great thickening of the horny layer of the skin.

(*b*) The *gummatous syphiloderm* is the most characteristic tertiary cutaneous manifestation. It appears either in the skin or subcutaneous tissue, as a pea- to walnut-sized, rounded, painless nodule—fixed to the skin when cutaneous, movable under it when subcutaneous. The gummata occur most frequently in the lower limbs and at the points where bone is directly covered by skin. The nodules increase in size; and, after a while, softening begins at the centre. The skin becomes reddened and finally may break, a sticky, tenacious, glairy fluid being discharged and a gummatous ulceration being formed. Gummata may, however, disappear without rupture, leaving slight traces behind them. They are usually few in number, although Lisfranc reported a patient having 150 at the same time upon the hands and legs. They occur late in the disease, but have been seen contemporaneous with the initial sore (Mauriac). Rhinoscleroma, carcinoma, and sarcoma have to be considered in the diagnosis of cutaneous gumma.

(*c*) The *ulcerative syphiloderm* is a later development either of the tuberculous or the gummatous eruption The shape of the ulceration is at first that of the preceding lesion; but the marginal extension is usually irregular, and ulcerations of the most varied sizes and shapes are thus produced. The base of the ulcer is irregular and covered by secretion which dries into crusts, forming the pustulo-crustaceous, the ulcero-crustaceous, or the rupial eruption. The ulcerations always result in scarring. They vary greatly in extent and number.

In the mucous membranes either the tuberculous syphiloderm or gummata may be seen. Softening and ulceration occur early, the lesion being most often seen in this stage. Its commonest site is the hard and soft palate; but it may also affect the tongue, pharynx, nose, vagina, etc. Tubercles and gummata also occur in the submucous tissue, where they form irregular, ragged ulcerations. The glossitis gummosa is a typical example.

**The Quarternary Stage.**[1]—Certain pathological changes, neither exclusively nor necessarily caused by syphilis, bear to the disease a relation long unrecognized, but now undeniable. They are not, as Fournier (who was one of the first to call attention to their relation to syphilis) puts it, strictly speaking of syphilitic nature, but they are none the less of syphilitic origin; and to them he has given the name metasyphilis or parasyphilis. Many, although not all, of them occur long after the initial lesion; and the syphilis in its early stages may have been quite benign and have run its course without incident. The two most striking characteristics of parasyphilis as distinct from syphilis itself are its total failure to respond to specific treatment and the fact that the clinical phenomena of affections parasyphilitic in nature differ in no way from these same affections when they are the result of

[1] The two following are the most useful works on this subject: (*a*) *Les affections parasyphilitiques*, by A. Fournier, Paris, 1894. (*b*) *Les affections parasyphililiques*, by S. R. Hermanides, Haarlem, 1903.

some other cause. Tabes, for example, may be either syphilitic or non-syphilitic; but it is the same clinical entity in either case. Notable also are the proneness of parasyphilis to affect the central nervous system and the gravity of its prognosis. The pathology of the condition is not, strictly speaking, a part of the pathology of syphilis as such; nor is the syphilitic origin of all of the "parasyphilitic phenomena" beyond dispute. The more syphilis is studied, however, the more convinced one becomes that it is not the self-limited disease it was once thought to be; and the more prone one is to consider as an etiological factor the remote luetic infection of which there is a history in so many cases of the affections which have come to be known as parasyphilitic.

(*a*) **Tabes.**—Tabes is the type, par excellence, of parasyphilitic affection. It was in 1875 that Fournier first taught that tabes originated in the majority of cases from syphilis. He was vigorously opposed by Charcot and the Saltpêtrière school, as well as by Leyden and Westphal; and the question as to the etiological relation of the two diseases has been discussed ever since, the opponents of the Fournier doctrine holding the occurrence of syphilis and tabes in the same patient to be a pure coincidence. There is no doubt about the fact that in the large majority of tabetic patients there is a history of syphilis, and that the percentage of tabetics who have had syphilis is much greater than the percentage of the healthy population who have had it. Erb found 89 per cent. of a series of 600 cases of tabes to be syphilitic; Fournier about 90 per cent. of 750 personal cases; and Marie says, "For all practical purposes tabes is always syphilitic in origin." At the same time Erb has found that tabes develops much more often in syphilitics in whom some of the other predisposing causes have been at work (exposure to cold, sexual excess, overwork, neuropathic tendency, etc.); and he regards syphilis not only as the most important, but as the necessary, etiological factor without which the "predisposing causes" cannot produce the disease.

Neither the clinical phenomena nor the anatomical findings throw any light on the question; for there is nothing about either that makes either for or against the luetic nature of the disease. The argument of Charcot and Leyden that tabes could not be luetic since it did not yield to specific treatment is not pertinent, and *absolute* proof of one or the other claim is still wanting; meanwhile, conclusions must be drawn from clinical data; and these, if not absolutely decisive, point so strongly to the etiological relation of the two diseases that the question may be regarded as settled. Certain of the cases of juvenile tabes have been shown by Strümpell and others to be the manifestation of hereditary syphilis.

(*b*) **General Paralysis.**—What has just been said in regard to tabes applies also to dementia paralytica. The etiological relation between syphilis and general paralysis of the insane was first suggested by Esmarch and Jessen in 1857; but the idea has since been staunchly supported by others. The line of argument is much the same as that used in the case of tabes and it is almost equally convincing; so that dementia paralytica must be considered among the parasyphilitic affections. Here again clinical facts seem to point also to a causal connection between juvenile general paralysis and hereditary syphilis. The very striking recent observations on the deviation of the complement in the study of the cerebrospinal fluid of patients with general paralysis (referred to below) apparently confirm completely the views of the Fournier school.

(*c*) **Nervous Affections.**—There is a whole host of other nervous affections which have been described as parasyphilitic, but their discussion belongs rather to neurology and they can only be mentioned here. Quite important is the syphilitic neurasthenia, more particularly the syphilophobia, which inspires the afflicted patients with a colossal dread of the disease, interprets every trivial subjective sensation as a luetic manifestation, and assures its victims that all the most horrid events of syphilis are to be their portion and their offspring's. Parasyphilitic epilepsy is also a fairly well-established clinical entity; and besides these are to be mentioned hysteria, Little's disease, and hydrocephalus among others.

(*d*) **Tongue.**—Parasyphilis frequently affects the tongue. It may take the form of fissures in persistent mucous patches or of recurrent herpes on the borders or dorsum of the tongue. But the common and serious lesion is buccal leukoplasia, which often degenerates into carcinoma, and is supposed to be most frequent in patients whose mouths have been subjected to the irritation of tobacco. In this condition the epithelial layers are thickened and hornified, the intercellular spaces roomy and filled with round cells. Keratohyaline drops (stained an intense red with picrocarmine and the sure sign of hornification) are present. The onion bodies, seen in epitheliomata, are often found in buccal leukoplasia. The adventitia of the vessels is thickened, there is proliferation of the connective tissue of the corium, and round-celled infiltration. The lymph and mucous follicles are also the seat of cell proliferation.

(*e*) **The Pigmented Syphilide** (syphilitic vitiligo or leucoderma), already described, may be regarded as parasyphilitic because it is not peculiar to syphilis (homologous eruptions being the chloasma of pregnancy, cachectic melanoderma, etc.) and because it resists specific treatment.

(*f*) The list of parasyphilitic affections may be almost indefinitely extended if one includes all the diseases in which syphilis is often an etiological factor, but against which antiluetic treatment is useless. The importance of syphilis in the production of amyloid degeneration, of arteriosclerosis, and of aneurism has already been referred to; diabetes insipidus is often associated with cerebral lues, and there are many more instances of suspicious association of this sort which might be mentioned.

**Congenital Lues.—Effect of Syphilis on Pregnancy.**—The first and most marked effect of syphilis on the fœtus is the interruption of pregnancy. In 330 syphilitic gravidities studied by Kassowitz, abortion or premature delivery occurred in 40 per cent. and only 60 per cent. reached term. The nearer conception is to infection, the greater the danger of interruption of pregnancy. Where many conceptions occur, however, in a syphilitic woman, the specific influence apparently "wears off;" the earliest pregnancies end in abortion, then dead children are born, then living children are prematurely delivered, then full-term syphilitic children, and finally full-term healthy children.

In pregnant women who are syphilitic, hydramnios is also frequent. The fœtus of a syphilitic woman either has macerated skin or, if born at term, presents the cutaneous lesions seen in adults. There are marked visceral lesions, particularly in the liver and spleen, which are much enlarged. The bones show the osteochondritis of Wegner, and the child has the pathognomonic "little old-man" facies and the other characteristics of hereditary lues to be described below. Placental changes are most marked when the

disease is contracted by the mother early in her conception. The placenta is large, weighing sometimes one-quarter as much as the fœtus. It is pale, œdematous, and either friable or firm. Microscopic examination shows placental cirrhosis with endo- and peri-arteritis and phlebitis of the chorionic villi. The umbilical cord also shows infiltration and vascular lesions.

The ill effects of syphilis on the children born of syphilitic parents may manifest themselves in three ways: (1) By faulty nutrition and various dystrophies; (2) by the actual signs of syphilis in the child at birth; (3) by the signs of the disease appearing some time after birth in a child born healthy.

1. **Dystrophies Syphilitic in Origin.**—The inaptitude for life transmitted by luetic parents to offspring, even when no actual syphilitic lesion is demonstrable in the child, may show itself in the intra-uterine death of the fœtus. When, however, the child reaches term, even in absence of definite signs of syphilis, the luetic dystrophies are often seen. Some of the children are born small, have no resistance to gastro-intestinal and other infections, and die early. Others survive; but they remain small, atrophic, and infantile, both in physique and intellect, have very slight resistance to tuberculosis and other infections, and are particularly subject to rickets. Faulty development and diminished resistance are the prominent characteristics of such children. Numerous malformations may, however, be added; but, although these are often seen in the children of luetic parents and seem to be syphilitic in origin, if not syphilitic in nature, it must be remembered that most of them may be and frequently are due entirely to other causes. These malformations usually affect the cranium. Asymmetry of the skull is often seen; large frontal bosses are not uncommon; and microcephaly and other variations of the head, both in size and shape, are observed.

Other characteristic deformities are seen in the face and mouth; for example, the flattened nose and the vaulted palate. Scoliosis and spina bifida are not infrequent. Polydactylism, syndactylism, congenital luxation of the hip, and flat-foot are some of the deformities of the limbs seen in the children of luetic parents. The heart valves are often faulty; congenital hernia is not rare; malposition of the viscera is occasionally observed, and incomplete development of testicles, breasts, and ovaries is sometimes seen. Retardation of intellectual development may be very slight, but quite often the children are slow in their mental grasp and lack attentiveness and memory; in some cases the children are congenital idiots. Deaf-mutism, deafness, strabismus, keratitis, malformation of the iris and other ocular structures are some of the deformities affecting the organs of special sense. One of the most characteristic malformations is seen in the teeth; this deformity was studied chiefly by Jonathan Hutchinson, and the "Hutchinsonian teeth" are still regarded as one of the very important stigmata. The change affects the median upper incisors of the permanent set of teeth. The teeth themselves are stunted and peg-shaped, their lateral borders being curved, and their axes usually converging from base to edge. At the free cutting border there is a single, broad, shallow, crescentic notch, or semilunar excavation. It persists for some years; but is finally obliterated by wearing down of the teeth. These changes described by Hutchinson are quite definite, and it is improper to call any malformed syphilitic teeth "Hutchinsonian teeth." The typical changes may, however, be absent and other malformations (not themselves peculiar, as the Hutchinsonian teeth are, to syphilis) may be seen. Transverse grooves and depressions are among the commoner changes,

the latter sometimes taking the form of the cupuliform atrophy of Parrot. Simple microdontism is sometimes seen.

With the exception of the Hutchinsonian teeth none of the dystrophies above described can be considered peculiar to syphilis.

2. **Early Congenital Syphilis** (*Syphilis héréditaire précoce*).—This is the most frequent form. The signs and symptoms are characteristic and the diagnosis is usually easy. Sometimes the disease is manifest at birth, but usually the child is born healthy and thrives until about the sixth week; occasionally the symptoms appear first about the sixth month. The typical facies described by Trousseau presents the following features: The skin is yellowish, the expression wretched, the eyelashes are wanting, the hair of the head scanty, and patches of alopecia are present; later, the appearance becomes the well-known one of a "little old man." The facies of Trousseau may be absent. The appearance of actual symptoms may be preceded by a period of restlessness and wakefulness. One of the first symptoms observed is the characteristic rhinitis known as "the snuffles;" this is a coryza with serous discharge, the formation of crusts, and resulting respiratory obstruction. The child usually at this time begins to nurse badly and nutritional disturbance supervenes. Ulceration and necrosis of the nose, with the formation of the saddle-shaped deformity, may occur. Fissures or rhagades appear at the corners or the free borders of the lips, increasing the wretched appearance of the child and greatly adding to the danger of contagion on the part of the nurse. Anæmia is present. The child goes from bad to worse; it suffers from malnutrition and often succumbs to cachexia. Many of the children are carried off by intervening acute infections, particularly bronchopneumonia and enteritis. Among good hygienic surroundings the prognosis is fair; otherwise it is grave, and in foundling hospitals the children practically all die. The glands are usually not enlarged; but a whole host of cutaneous lesions, including most of those seen in syphilis of adults and certain others peculiar to the congenital form, appear. Their severity is a clinical characteristic.

*The roseola* is usually wanting; but a yellowish-red, maculopapular erythema, beginning on the buttocks and thighs and extending to trunk and face, is sometimes seen.

*The psoriaform syphilide* is very characteristic. It consists of bright-red or copper-colored, infiltrated areas on the palms of the hand and soles of the feet, covered by white, dry scales, which are easily detached, leaving a collarette at the periphery. It corresponds to the psoriasis palmaris and plantaris syphilitica of adults.

*The erythema*, when situated about the body orifices is usually accompanied by *rhagades*. These are true ulcerations which may leave indelible scars, particularly characteristic being the ray arrangement about the lips and chin.

*Mucous patches* occur in the mouth and about the lips; but they show a predilection for the intergluteal groove, the perineal, genital, and genitocrural regions. This may be due in part to the constant irritation by urine and fæces in these sites. There is, however, very little tendency to condylomatous overgrowth, as in adults. Patches are also seen back of the ears and near the nose, where they are often covered by crusts.

*Pemphigus neonatorum* is the most characteristic of the cutaneous lesions. This syphilide is most often situated on the palms of the hands and soles of the feet. It may be present at birth, or, if appearing later, it begins as a

bluish-red infiltration; the epidermis is soon raised and vesicles and bullæ are formed. Sometimes, however, there is no liquid present. The lesions are 2 mm. to 1 cm. in diameter. The epidermis is white, as if macerated, and lies in folds; below, the skin is reddish, wine-colored. The serous exudate soon becomes purulent, by the invasion of fusiform and round cells and leukocytes; the vesicles become tense and are either absorbed or burst, leading to purulent ulcers, which are often serious. In malignant cases there is extensive destruction of the skin, with gangrene, necrosis, and, not infrequently, death.

*Hemorrhagic Exanthemata.*—Syphilis is a well-recognized cause of hemorrhage in the newborn and not infrequently this occurs subcutaneously (syphilis hæmorrhagica neonatorum). The hemorrhages may be subcutaneous or submucosal; sometimes they occur about the umbilicus. Of 3364 children studied by Wilson[1] at the Philadelphia Lying-in Charity, 10 died of hemorrhage attributable to syphilis. Reduced coagulability of the blood and increased arterial tension in the newborn are the causes assigned by him. Jaundice was practically always present in some degree.

*Acne syphilitica, impetigo syphilitica,* and *ecthyma syphilitica* are three self-descriptive exanthemata more or less characteristic of the congenital form of lues. The *poorly nourished skin* of children afflicted with hereditary lues is also subject to many skin affections not themselves specific. Eczema intertrigo is, for example, quite common; and suppuration and destruction of the nails is not infrequent.

*Bony changes* are frequent and characteristic. The dystrophies of the cranium, particularly the frontal protuberances, have already been mentioned. In the limbs they often manifest themselves in the syndrome of Parrot (syphilitic pseudoparalysis of the newborn). This is characterized by immobility, pain, bony swelling, and sometimes crepitation at the epiphyseal line. There is no true paralysis, the muscles reacting to faradism and galvanism. It usually affects only one limb, but sometimes two. It may be the first sign of congenital lues; but more often appears in the third or fourth month.

*Osteochondritis syphilitica,* first described by Wegner, is highly characteristic of congenital lues. Its site is the boundary between diaphysis and epiphysis of the long bones (upper end of the tibia and both ends of the femur particularly) and between bone and cartilage in the ribs. Three stages are recognized. In the first there is marked proliferation of cartilage cells at the boundary of the diaphysis, forming a zone recognizable macroscopically between diaphysis and epiphysis. Within this zone ossification is irregular and retarded. In the second stage proliferation of cartilage cells advances and there is further irregular ossification at the epiphysis. In the third stage one finds bulgings of the cartilage, with thickening of perichondrium and periosteum. The cartilage forms a broad, irregularly limited zone; the portions next the spongiosa consist of a pus-like, semifluid mass. Epiphyseal separation may occur.

*Rickets* was regarded by Parrot as merely an expression of hereditary lues. This view cannot be maintained; each is an independent disease; yet there is little doubt that congenital syphilis predisposes to rickets and that the two conditions are frequently combined.

[1] *Archives of Pediatrics,* vol. xxii, p. 43.

*Visceral lesions* are observed in practically all the organs of congenitally syphilitic children. Many of them are without characteristic symptoms; diarrhœa and vomiting occur, but they are not pathognomonic. Involvement of the testicle is, however, particularly characteristic; and orchitis with exudative vaginitis in an infant is always suggestive of lues. It usually ends in sclerotic atrophy. The enlargement of liver and spleen are also of clinical importance from the aid they give to diagnosis. The former is regular, smooth, and very large, reaching sometimes to the iliac fossa. It is cirrhotic, but the cirrhosis is usually unaccompanied by circulatory changes or icterus. The large, palpable spleen is also of diagnostic import. Affections of the eye are seen in the early form of hereditary syphilis, but interstitial keratitis is much less frequent than in the late form.

3. **Late Congenital Syphilis** (*Syphilis héréditaire tardive*).—This form, especially studied by Hutchinson and others, has been clinically well recognized only in comparatively recent years. Its manifestations were formerly either regarded as those of acquired syphilis or dismissed as "scrofulous." It appears usually about the time of the second dentition or at puberty, and is most frequent in those who have shown signs of the early form in infancy. It occurs also, however, in patients whose childhood has been free from disease. Its manifestations are not often seen after the twenty-eighth year; but a terminal time limit is, of course, difficult to set. Any organ in the body may show syphilitic manifestations of a gummatous, sclerous, or sclerogummatous type; but the following are those most often affected: the eyes, the bones, the skin, the throat, the pharynx, the brain, and the ear. One of the most important changes is the almost pathognomonic interstitial keratitis. This usually occurs between the eighth and fifteenth year, and begins as a diffuse haziness near the centre of the cornea of one eye. It is accompanied by some irritability of the eye and by dimness of vision. When looked at more closely the corneal haziness is seen to consist of discrete, punctate deposits within the cornea itself and not on its surfaces. In a few weeks the whole cornea becomes involved, takes on the appearance of ground-glass, and is surrounded by a zone of ciliary injection. Photophobia becomes a symptom and involvement of the opposite cornea takes place. The vision is quite dimmed; but soon the condition begins to improve and the cornea clears slowly. If the case is treated early, the prognosis is fair and is inversely proportional to the degree of photophobia. Recovery is, however, always slow and, at best, imperfect.

The cutaneous and mucous lesions of late congenital syphilis in general resemble those of acquired lues. Fissures and rhagades occur about the mouth. Changes in the bones are a marked feature of the disease. Bosses are seen on the skull, and hyperostoses on the long bones. The sabre-shaped tibia is particularly characteristic; here the bone is much bowed and is increased in volume by a chronic osteoperiostitis accompanied by gummata. The latter often break down and ulcerate. Arthropathies are occasionally seen, particularly a form of synovitis which resembles white swelling; and a special form of symmetrical synovitis of the knee has been described by Clutton.

In typical cases the whole clinical picture is characteristic. The patients are small and poorly developed; the skin is of an earthy paleness; the forehead is prominent, the frontal eminences marked, and the skull asymmetrical; the bridge of the nose is depressed and its tip *retroussé;* there are cicatricial

stigmata of the skin and mucosæ, and striæ about the mouth; there is the presence of the Hutchinsonian triad (pathognomonic alterations of the teeth, interstitial keratitis, and disturbances of hearing); there are signs of infantilism (slender physique, undeveloped testicles, rudimentary beard, and pubic hair); there is glandular enlargement, often mistaken for tuberculosis; and finally there is arrested intellectual development. Further confirmation of the diagnosis may be obtained by inquiry into the family history, which will often show a high mortality or a high percentage of abortions; and, by confrontation, revealing the source of the disease in one parent or both. The general clinical picture has been well drawn by Augagneur: "Had I in a few words to present the ideal, clinical type of late hereditary syphilis, I should select a young girl, eighteen or twenty years old, whose eyes should present traces of parenchymatous keratitis; the teeth should be eroded and crescentically notched; at the same time they should be small and irregular; the hearing should be partially or totally lost in consequence of frequent attacks of otorrhœa; the genitals, possessing all the attributes of virginity, should be small, the mons veneris and the axillæ should be smooth; the mammæ without prominence, and menstruation should scarcely be established. Add to these all the tertiary lesions you please and you will have before you a complete picture of late hereditary syphilis. . . . To the triad of Hutchinson—interstitial keratitis, defective incisors, and deafness—I propose to add two other signs: general congenital atrophy and general arrest of development."

**Prognosis.**—Syphilis is a curable disease. It is not, however, *always* cured even by the most efficient treatment; and there is unfortunately no way of determining with exactness whether treatment in a given case has been sufficient to warrant us in a dogmatically favorable prognosis. We have only empirical results to go upon; but the clinical records of large series of cases carefully studied over long periods of years justify the following conclusions as to the outlook for a luetic patient:

1. In general, the prognosis for the average case is good with prolonged treatment and bad without it. This holds for the secondary phenomena, for tertiarism, and for the transmission to progeny.

2. No deduction as to the virulence of the disease is to be drawn from the character of the chancre; phagedenic sores may introduce a mild syphilis and herpetic chancres a malignant one. Nor do the secondary symptoms *per se* give us any indication of the future.

3. The prognosis improves with the promptness of the institution of treatment and seems to depend pretty directly on the vigor and intensity of the early mercurialization. The secondary period, if the sore has been positively diagnosed and treatment promptly begun, is as a rule only manifested by a few benign symptoms; on the other hand, cases first treated in the tertiary stage are difficult and often impossible to cure.

4. The frequency of tertiary symptoms, other things being equal, is inversely proportional to the adequacy of treatment received.

5. A patient who has received the thorough treatment outlined below is entitled to consider his disease cured and himself a safe husband and father. We cannot, however, *guarantee* that no syphilitic or parasyphilitic phenomenon will manifest itself. We can only say that such an occurrence is extremely improbable. "Neither the dose," said Ricord, "nor the pharmaceutical preparation, nor the duration of treatment, confer immunity

with certainty or guarantee the complete and radical extinction of syphilis." For this reason a patient who has had syphilis should never be dismissed from observation; and he should be advised of the importance, in case of future disturbance of health, of informing his physician of his syphilitic antecedents.

6. Three types of syphilis may be recognized, according to course and prognosis. *Benign syphilis*, which is even occasionally seen in untreated cases, occurs most commonly in women. Here the initial lesion, a mild sore throat, a moderate roseola, and an adenopathy, perhaps with headache, make up the entire symptom-complex. *Normal syphilis* shows well-marked but not severe symptoms throughout, and the manifestations are quite amenable to treatment. After a certain time, during which a number of relapses and exacerbations occur, the disease ends, although parasyphilitic phenomena may later appear. *Malignant* or *galloping syphilis*, less frequent now than formerly, presents either the normal manifestations in severe, frequently recurring, and obstinate form, or else violent, often rapidly fatal tertiary manifestations early in the disease. The skin eruptions are ulcerative and pustular; cachexia is marked; gummatous lesions are extensive and occur early, and the internal organs are rapidly involved.

7. Hereditary syphilis offers in general a very bad prognosis. The average mortality is probably about 75 per cent. Kassowitz states that one-third of all syphilitic infants die *in utero*, and of the remainder 34 per cent. succumb during the first six months of life. Here, again, treatment affects the prognosis wonderfully; according to Étienne 95.5 per cent. of living syphilitic children die if untreated and only 10 per cent. if properly cared for.

**Syphilis and Marriage.**—Syphilitics may marry with safety after they have undergone three years of thorough treatment and have been without symptoms at least one year after treatment has ceased. Hutchinson thinks that in women who have suffered from acquired syphilis the liability to transmit to offspring lasts much longer than it does in men.

**Syphilis and Insurance.**—The relation of syphilis to the problems of longevity gives this disease great importance from the standpoint of life insurance. It is very difficult to estimate the percentage of deaths actually due to syphilis; but the vital statistics published by the *United States Census Bureau* make it seem probable that the fatality is about 2 per cent. (Hyde). Runeberg, of Helsingfors, on the other hand, found that 11 per cent. of 734 deaths of insured persons were due to diseases resulting from syphilis; and that if certain apoplexies, probably syphilitic, were included the syphilitic mortality was 15 per cent. of the total, being second only to tuberculosis which caused 21 per cent. of the deaths. These figures assume added importance when it is remembered that they represent the facts existing among the insured—that is to say, the most vigorous portion of the population. Chronic alcoholism, long-continued tobacco narcosis, extreme fatigue, severe affliction, poverty, and the stress of anxiety are well-known contributing factors to the serious effects of syphilis. The diseases most commonly causing death after syphilis are affections of the heart, general paralysis, diseases of the central nervous system, chronic nephritis, and aneurism.

The damage wrought by syphilis consists, however, chiefly in its lowering the standard of average health, paving the way for other diseases and possibly laying the foundation for mental degeneration and alienation. The expectation of life after acquired syphilis is in large measure affected by the inherited

tendencies, the habits of life, and the environment of the individual. The longevity prospects are undoubtedly better for women than for men. The ideal applicant for life insurance who has suffered from syphilis should have had active and unmistakable symptoms early in life; he should have had, after efficient treatment, several years' exemption from all evidences of infection; he should have an excellent family history, particularly as regards nervous diseases; and he should lead a life relatively free from strain, excess, indulgence in alcohol and tobacco. Most insurance companies require that four or five years shall have elapsed since the disappearance of the last symptoms of the disease; and no applicant who has had syphilis is given a policy which will keep him on the company's books after his fifty-fifth year. The frequent occurrence of arteriosclerosis in middle life among those who have had syphilis suggests the possible practical value of studying the blood pressure of these applicants for insurance with regard to increased arterial tension at the time of application (Hyde).

**Prophylaxis.**—There are many striking things about syphilis, but none is more striking than its persistence in spite of knowledge complete enough to stamp it out. It is a disease almost unparalleled in the extent and intensity of its ravages; it is the subject of popular dread; yet it is both preventable and, within limits, curable. Metchnikoff has called attention to the strange fact that medicine has been able to restrain, in some cases almost completely, infectious diseases transmitted by flies and mosquitoes, but that in tuberculosis, lues, and other diseases carried about by man and transmitted without intermediary, prophylactic measures have been attended with great, almost insuperable difficulties. In these instances both receiver and transmitter of the disease are reasonable beings; and if, as is the case in syphilis, an absolutely sure prophylaxis were known (congenital and innocent syphilis are for the moment left out of consideration) one might expect that the disease would be as easily and completely eliminated as typhus, for example, has been. It is true that syphilis, where it exists at all, is less prevalent among civilized than among uncivilized peoples; in Siam, for instance, uninfected individuals are said to be considered rareties. Yet even civilization has not done for syphilis what it did for smallpox. In Paris, out of every 100 men at least 13 to 16 infected individuals may be counted; and Paris is only mentioned as an example. The number of days on which soldiers of the English army were incapacitated from duty on account of syphilis has become nearly trebled during the years from 1880 to 1897, while the number of men has only been doubled in that period. The reason for this persistence of misery in the face of information complete enough to prevent it is of course not far to seek; it lies in the Social Problem, with which the problem of syphilis is so intimately allied. And it is therefore essential to an understanding of the hygiene of syphilis that practising physicians, since it is they who must face the problem which belongs equally to the State, become familiar with the facts of the case and with the various solutions suggested.

The problem of syphilis is essentially the problem of prostitution. More exactly, it is the problem of clandestine prostitution. This is the source of the disease; and inasmuch as elimination of this source is beyond the dream of all, the question which the physician has to answer is a double one. First, How can clandestine prostitution be best kept within limits and made least harmful to the common weal? Second, How can the public best be kept advised of the danger to itself of prostitution and be made to escape

that danger? The prophylaxis of syphilis includes, therefore, public and private hygiene. Public hygiene has concerned itself with efforts aimed directly at prostitution, with efforts aimed at syphilis itself, and with efforts aimed at society itself, by way of education, institutional reforms, etc.

1. **Public Prophylaxis Dealing Directly with Prostitution.**—One hesitates to approach this subject because of the very varied opinions which have existed and still exist about it. Relentless abolitionism on the one hand and equally relentless State control on the other have been enthusiastically supported. The whole question, indeed, of the relation of the State to the industry of prostitution is beset with difficult problems at every step; yet men impressed with the injury to the commonwealth which prostitution involves have always been tempted to turn, as they are tempted to turn in other similar dilemmas, to a State fiat for the panacea sought. State interference with prostitution is no new procedure. In Athens prostitutes were denied the right of citizens, the Areopagus oversaw and punished them; they were given a certain part of the city for their dwelling and made to wear a particular costume. Similar laws prevailed in Rome, where the "licentia stupri" was a State permission of the industry. This seemed to these enlightened governments the best solution of the problem, and since those ancient days many students of the question have thought similarly; others, however, have maintained that recognition of an institution well known to be detrimental to public health was no business of the State; and between these two sides a lively battle still rages. Statistics unfortunately have given little assistance in deciding the dispute. The presence of venereal diseases may be exceedingly difficult to demonstrate in women, so that the exact extent of syphilis is impossible to know at any given time. The extent of prostitution, a large part of which is always clandestine, is equally impossible to determine, and its prevalence is so influenced by other factors (state of public opinion, character of population, etc.) as to make it difficult to reason from its diminution or increase to State interference as the cause.

There have been three parties as to the attitude the State should assume toward prostitution. The first has maintained that prostitution should be under State control; the second, that prostitution should be prohibited by the State; and the third that no State regulation should exist. Each one of these views has been put in practice. State control was given an early trial in Belgium; prohibition was attempted in Bavaria in 1861; and in various European countries all theories of the State's attitude toward prostitution have been tested.

(*a*) *State Control of Prostitution.*—Where this obtains, the industry is recognized by the government as a necessary one; it is, however, also recognized as a dangerous one, and its practice is permitted only under governmental supervision. Essentially, it consists of (1) inscription of prostitution, either voluntary or forced; (2) permission to ply the trade under certain regulations; and (3) governmental medical inspection, with obligatory treatment. Control of this sort, on the part of the State, has been attempted in many forms. Simple State regulation (*Kasernirung*) and the establishment of brothel streets (as in Bremen) are the three forms at present in vogue, and each has its staunch adherents and equally staunch opponents. Fournier in his latest book argued strongly for State control. He recognizes its limitations and states that "it is definitely proven, from long experience, that the administrative and police measures which constitute the present

system are insufficient to defend us against syphilis." Nevertheless, he concludes, from a thorough-going analysis of the question, that regulation is necessary in the public interest. It should include medical examination of all women convicted of professional prostitution and internment of these women in case of contagious disease. The supervision should, however, be carried out in a legal way; it should aim also to be humanitarian and charitable.

(*b*) *Abolition of State Regulation.*—Von Düring, on the other hand, an exceptionally well-informed, enthusiastic, and logical writer on the subject, relentlessly opposes State regulation of prostitution for the following reasons: (1) The medical supervision is necessarily incomplete and therefore gives a false sense of security. (2) The industry is one which leads to much misery and the State should have no hand in it. (3) The number of prostitutes in a given community cannot possibly be even estimated approximately; the greater part of prostitution is clandestine; and for these reasons it is absurd to talk of regulating it. (4) State regulation is contrary to the Constitutions of the Governments which forbid pandering. (5) There is no need for brothels; this is proven by the fact that they are actually diminishing in number in most of the Continental cities; and that at best the inmates of them represent a very small fraction of the total prostitution of a community. (6) Brothels are a danger to the State. They are morally unsound, as enticing to youth and teaching them that illegitimate intercourse is safe. They offer allurements particularly to unripe youths and to the intoxicated. They mean slavery and a most dreadful existence for the inmates; and they are the breeding places of sexual perversions. They do not clear the streets, as is proven by the small percentage of the total prostitution of a community living in them. (7) Examination of prostitutes for venereal diseases is no function of the police; and it is unjust, because it includes only women. (8) Almost everyone who is well informed on the subject is against regulation. (9) State regulation, after a fair trial, has done nothing in diminishing the occurrence of venereal disease; it has been a practical failure. (10) To these arguments may be added that of Josephine Butler, the famous English abolitionist: morality comes before every other consideration; hygiene only comes in the second place; "if the safeguard were as real as it is fallacious it would in no way render regulation legitimate" (P. W. Bunting).

It is obviously difficult to come to a conclusion in a question where experts are at such disagreement. Certain facts are, however, to be taken as settled. State regulation has been a very small factor in the fight against venereal disease, even granting its exponents' claim that it has been a factor at all. And it is supported by very few of those venereologists whose opinion is entitled to consideration; in France, the home of regulation, a recent Commission by a majority of 60 to 5 adopted, among others, the following motion: "The regulation of prostitutes is to be condemned."

The question of State regulation of prostitution, it must, however, be insisted, is really one of the minor problems connected with the problem of the prophylaxis of syphilis. Governmental supervision deals, as has already been said, even under the most ideal conditions, with an almost negligible fraction of the total prostitution, and from the very nature of the case leaves untouched the clandestine prostitution which is spreading disease. It is, furthermore, absurd to ask much of it, when it is remembered that law is only effectual as an expression of the predominating opinion of the common-

wealth; and to expect, as has been expected, that State regulation subdue prostitution in countries where the mistress is not simply a tolerated but a well-recognized and accepted personage, where promiscuous intercourse not only thrives, but has actually created for itself a literature, where the marital tie is regarded in the loosest way, is like sowing weeds and then asking for a law that no weeds shall grow.

We have then to consider those aspects of the public hygiene of syphilis not directly concerned with the attitude of the State toward prostitution.

2. **Public Prophylaxis Concerned with Syphilis Itself.**—(*a*) It has been suggested, first of all, that the disease be made a reportable one and that treatment be obligatory. Aside from the very large problems which this procedure would create as to a physician's right to reveal a professional secret of this nature, it seems quite certain that a regulation of this kind would rather hinder than promote proper treatment of the disease. Enforced publicity would certainly lead to the concealment of syphilis, and many cases now well treated would go untreated.

(*b*) The establishment and maintenance of proper institutions for the study and treatment of venereal diseases is a crying need everywhere; and the commonwealth can do nothing better for the common weal in the matter of syphilis than by making this necessary hygienic provision. This is a part of the fight against the disease which has been wofully neglected; it is a part which should receive the support of every well-informed physician, as offering a well-grounded hope of accomplishing much in the attempt to eliminate the sources of infection and to diminish the miseries of the already contracted disease. The cure for syphilis is known; if it is not applied, the fault lies with the community which chooses to make no use of its knowledge; and of this blame the medical profession must accept a large share. "Before having recourse," wrote Mireur in 1874, "to extreme procedures, before extolling Utopian projects, it would be rational to demand that those most elementary measures be carried out without which every effort is vain." The "elementary measure" of hospitalization and efficient treatment was then in a sorry enough plight. In England and on the Continent the provision made for the treatment of venereal disease was ridiculously inadequate and patients were actually "abandoned to be devoured by the disease like fodder."

The progress of the last thirty years has not made anything like adequate provision for syphilis. "The number of beds," said a Commission of the French Academy of Medicine, "provided for cases of venereal disease is notoriously insufficient;" and this puts the case only mildly for other countries than France. Yet the prophylactic value of adequate therapeutic provision in the case of syphilis can hardly be exaggerated. "Let us suppose," wrote Acton, "that a syphilitic woman has no money for treatment and cannot be admitted to a hospital; does anyone believe that she will die of hunger in order to avoid the risk of infecting the drunken laborer with money in his pocket? What happens? Her disease grows worse. . . . The drunkard, whom she has infected, is a husband, who gives the disease to his wife and by her the suckling is infected. The father does not dare to confide to his wife the nature of the disease; and the wife, ignorant of its consequences, leaves it to work out its ravages. Soon the whole family, unable to supply its needs by work, becomes a parasite, for months at a time, on public charity. Every year death harvests a large number of children infected in this way;

and he who has closed the hospital doors to the disease has done nothing else than send away the pestilence which hastens, with rapid steps, into the shadows."

It is not, however, by real hospitalization that the disease is best treated and cured. Hospital wards, where selected cases can be sent, are badly needed, and the present deplorable inadequacy of hospital provision for syphilis cannot be too heartily condemned. But the crying need is for efficient venereological dispensaries. These should be numerous; they should be systematically distributed, so as to save patients loss of time; the consultations should be at convenient times and every effort should be made to render the dispensaries easy of access; they should furnish instructions as to prophylaxis against the disease and the necessary measures to prevent its spread; they should be conducted humanely and with due regard to the feelings of patients in this matter; and they should, of course, be manned by well-trained venereologists. This is a part of the public prophylaxis against syphilis which physicians should insist on; it is a rational, promising, and feasible procedure.

(*c*) *Antisyphilitic Vaccination.*—Experiments with this method of prophylaxis have not been very satisfactory and the procedure must develop greatly before any State interference of this sort promises to accomplish what compulsory vaccination against smallpox has brought about. Various sera have been used: blood serum from syphilitic subjects in the secondary or tertiary stage, serum from heredosyphilitic subjects, serum from the secretions or pathological liquids of syphilitic subjects, serum of animals inoculated with various syphilitic products. The discovery of the spirochæte of Schaudinn may throw some light on the subject; but unfortunately this protozoan belongs to a group difficult or impossible to cultivate on media hitherto employed, and much progress must be made before a practicable method of cultivating the syphilis spirochæte on a scale large enough for these purposes is obtained. Levaditi has, however, succeeded in cultivating two analogous spirilla, those of fowl septicæmia and of relapsing fever; so that the cultivation of the spirochæte of Schaudinn does not seem entirely out of the question.

The outlook as to the prophylaxis of syphilis by the serotherapeutic method is not, for several reasons, very good. The early endeavors of Richet and Héricourt with defibrinated blood were failures; nor were the experiments of Roux and Metchnikoff with subcutaneous and intravenous injections of serum from syphilitic patients encouraging. A mode of prevention by means of true vaccines might have a better chance of success; but here again one meets the same practical difficulty, inability to obtain the pure virus in sufficiently large quantities. Certain experiments of Metchnikoff and Roux made in 1903 seemed to show that the syphilitic virus, if passed through macaci, became much attenuated both for the macacus and for man; and it is not at all out of the question that inoculation with an attenuated virus may in the future be an important feature of the prophylaxis of syphilis. Even at best, however, the prophylactic use of antisyphilitic vaccine seems destined to be limited. The use of a living syphilitic virus on a large scale might bring about awkward complications, tabes and general paralysis, for instance, being frequently seen after very mild syphilitic lesions; and the great frequency of exposure to infection would offer a practical difficulty in the use of virus not experienced, for example, in the case of

diphtheria. Vaccination might be applicable to the uninfected children of luetic parents, and this mode of transmission might be thus prevented. On the whole the method of prophylactic vaccination, although it is no Utopian scheme, offers at present little beyond the hope that the discovery of the causative organism of syphilis and the increasing knowledge of experimental syphilis in animals may lead to useful development in serotherapeutics.

Already the study of experimental syphilis along the lines of immunization has led to what is apparently an important discovery from the standpoint of diagnosis, and on it the following diagnostic test for syphilis is based:[1] Syphilitic material from monkeys which have received treatment is mixed with the material to be tested and complement (fresh guinea-pig serum) added. To this mixture one adds specific hemolytic serum and red blood corpuscles. If the material to be tested is luetic, hemolysis ceases or, at least, is diminished; if it is not luetic, hemolysis proceeds. In the former case the amboceptor in the luetic material to be tested unites with the receptor in the known immune syphilitic material; the two together cause diversion (Ablenkung) of the guinea-pig complement, and the reaction results. If, however, the material is *not* luetic, no combination of amboceptor and receptor occurs, there is no diversion of the complement, and the reaction is absent. The cerebrospinal fluid of 8 cases of general paralysis has been recently examined in this way, and the luetic antibodies were always found. Other non-luetic cases similarly examined were negative.[2]

The vaccination of persons suffering from hard chancre against the occurrence of secondary symptoms has been experimentally studied by Kraus and Spitzer. Their first results were encouraging, but Brandwenier and others finally proved that secondary symptoms could not be prevented in this way.

3. **Public Prophylactic Efforts Concerned with Society and its Institutions.**— Procedures of every sort have been suggested according to which the prophylaxis of syphilis was to be strengthened by some change in the legal attitude of the State toward the disease or by an alteration in the institutions of Society.

(*a*) Penalty for the transmission of syphilis has been proposed by some as a necessary and important step in the attempt to destroy it. The infection with the disease, it has been urged, is a distinct bodily injury knowingly inflicted, and it should be subject to legal punishment just as assault and battery is. Quite aside from the constitutional question involved as to what constitutes a bodily injury, the practical difficulties in the way of ascertaining with certainty the source of infection, and proving that the disease was maliciously transmitted, render this suggestion wholly futile except in rare instances.

(*b*) Should the transmission of syphilis from husband to wife or from wife to husband constitute grounds for divorce? And should its existence in either party be prima facie evidence of adultery. These are difficult questions which belong rather to law than to medicine; yet they are questions which cannot be disregarded in considering the prophylaxis of syphilis. The hideous injustice to which a husband or a wife submits when he or she

[1] Wassermann, Neisser, Brucke: *Deutsche med. Wochenschr.*, 1906, Nr. 19, 10.
[2] Morgenroth u. Stertz: Nachweis der syphilitisch. Antikörper u. s. w. *Virchow's Archiv*, Band clxxxviii, Nr. 1.

is knowingly and voluntarily infected, by the other party, with the disease tempts one to provide legal redress for the predicament. Yet the procedure is a dangerous one; its application would present great practical difficulties, and it is doubtful if it would often be taken advantage of by the injured party.

(*c*) It has also been urged that a certificate of health as regards venereal disease be required before marriage permits are issued. Once more, practical difficulties loom large. The right of the State to invade this domain is not generally conceded, and the right of the physician to reveal professional secrets of this sort is pretty generally questioned. Furthermore, this sort of an alliance between medicine and the police, aside from its being an infringement on the dignity of the medical profession, would offer opportunity for all sorts of abuse. Upon one point, however, there can be no doubt. It is the bounden duty of every physician to use every means in his power to prevent marriage between people with venereal infections. He should absolutely forbid his syphilitic patients to think of this step until they have undergone proper treatment, and he should enforce this command with complete information as to the dire misery sure to result from such a marriage.

(*d*) Sanitary examination of men. (1) Such an examination, together with obligatory treatment, already obtains among certain government employees, as, for instance, in some armies and navies. Diday maintained that it should apply to all government servants, and the method of attacking syphilis by requiring all civil service employees to undergo examination has been strongly urged. It has also been suggested that all public wards (tramps, beggars, and prisoners) should be submitted to examination for syphilis. Over the army and navy the government can, of course, exercise a legitimate control; and strict hygienic provision should be made for restricting the occurrence of the disease and limiting its bad effects in every way. This is all the more necessary when one remembers how important a factor soldiers and sailors are in the transmission of syphilis; and hygienic regulation of this sort would accomplish much more if strengthened by international agreements as to the hygienic care of sailors and soldiers in foreign parts. The extension, however, of such a governmental oversight to the civil service and even, as has been urged, to private assemblies of workmen in factories and elsewhere, besides presenting great practical difficulties, represents a paternalistic attitude that would receive scant support from the community. (2) The examination of customers on their entrance to brothels has been seriously urged by certain writers as a promising procedure in preventing syphilis. The idea is no new one. As early as 1430 there was a regulation requiring such an examination in London, and Diday was a strong supporter of the idea. It was tried for a while in Hamburg. The scheme is, of course, quite out of the question; for it would be perfectly impossible to find reputable physicians who would give their time to such business; and in the hands of any but such physicians it would lead to all sorts of graft and abuse. Furthermore, as Ricord showed, it would simply result in an increase of free prostitution: "Aside from the difficulties of such an arrangement, the dangers which one wished to prevent by it would be increased; for instead of falling into a sewer which the police could cleanse, the filth would go elsewhere."

(*e*) It is notorious that venereal diseases furnish a large percentage of the material of charlatanism. In the case of syphilis the insufficient and unintelligent, if not actually dangerous, treatment which results is a definite menace to public health, and war on charlatanism is therefore a distinct

part of the prophylaxis of syphilis. Nowhere can neglect or ignorance bring greater misery, and most often to the innocent, than in the case of this disease; that its care should be in competent medical hands is therefore essential to the public health. Provision for its treatment in adequate venereological dispensaries is one phase of this prophylactic measure; but legal provision against the industry of quacks, a provision to which the public, with strange neglect of its welfare, is indifferent or even hostile, is an equally important feature in guarding against it.

(*f*) There are certain industries (glass blowing is one of them) notoriously dangerous in the transmission of syphilis; and it seems to be well within the power and duty of the State to see to it that proper hygienic supervision is exercised. That vaccination should be under rigid oversight in this respect goes without saying; and the possibility of infection by surgical or dental instruments is one that has but to be mentioned in these days of careful technique. One should insist, however, on the very great care necessary in venereological dispensaries where chancres are being constantly handled and circumcisions frequently done, for this operation has more than once been responsible for the transmission of the disease.

(*g*) Education, the sovereign balm in so many other instances, offers the greatest hope. Here is a disease bringing untold misery to a large proportion of the community, rendering great numbers of citizens inefficient, and transmitting its calamities to wholly innocent parties. It is a disease the phenomena and far-reaching miseries of which are known with certainty; it is a disease which can be perfectly well avoided; it is a disease which, when contracted, can be greatly limited both in its early manifestations and its late effects. Yet it is a disease about which even the educated classes are wholly uninformed or wofully misinformed; while the masses depend for their information on the unintelligent mouthings of alarmist quacks.

1. *Education of the Medical Profession.*—Students are rarely well instructed in syphilis; they are almost never thoroughly instructed. "This explains," writes Fournier, "why medical men mistake chancres and mucous patches for something else; why they give syphilitic infants to the care of a healthy nurse, or inversely; why they regard syphilis as cured after a few months or even weeks of treatment, and why they permit marriage to uncured syphilitics." In no way, indeed, does the public health suffer more when medical errors are made than it suffers if the errors be made in regard to syphilis; and these are errors which might be avoided by adequate attention to the subject in medical curricula.

In England there is not a single chair of syphilography; only recently has attendance on a clinic for syphilis been required in Germany, where many universities are without chairs of syphilography and where not a single full professor of dermato-syphilology exists; in America, in Austria, in Italy, even in France there are similar complaints; while only rarely do the departments of skin and venereal diseases possess the equipments deemed necessary for the treatment of other diseases. The establishment of adequate venereological dispensaries is, therefore, an educational need of the greatest importance; and attention to the public health demands that the instruction in regard to syphilis should be improved in the universities. Every candidate for a degree in medicine should be required to have attended at least a three months' special course in venereal diseases and to have passed a rigorous examination on this subject. Furthermore, the clinical material

of venereal wards and dispensaries should be utilized for the instruction of students and for the investigation of the disease. "If the sexual diseases are to be subdued," writes von Düring, "every single practising physician must be sufficiently instructed along these lines."

2. *Education of the Laity.*—This procedure is a delicate and difficult one. Certain suggestions may, however, be made as to possibly valuable educational undertakings.

(*a*) The first need is that the dangers of syphilis, about which the laity has the vaguest ideas, become matters of public knowledge. It is, of course, idle to expect that such knowledge would entirely protect the public from contagion; for those who are to be deterred from debauch by no consideration of public or private hygiene would continue to contract and to spread the disease. There are, on the other hand, certain people who are absolutely protected from danger by a thorough knowledge of it; and it is the duty of the medical profession to see that such persons, however small a part of the community they form, do not have to purchase their knowledge at the price of experience. Just how this knowledge is to be spread is a matter for consideration on account of the unique delicacy of the task. No doubt one of the functions of a venereological dispensary is that of instruction; and it would probably be useful to have printed guides distributed from these centres in somewhat the same way as is now done for tuberculosis. Much work is being done along these lines, and there seems no good reason why the public should not be given this information in popular magazines and similar ways. For it must again be emphasized that the problem of syphilis is one which each nation will have, sooner or later, to meet. The dangers of syphilis are essentially dangers to the commonwealth; and the commonwealth should be instructed about the disease itself, about the value of adequate treatment, and about the great risk of neglect.

(*b*) It is also in the interest of public health that the community should understand the dangers of prostitution. Instruction in this matter, by reason of its difficulty and delicacy, offers hope of doing good only when given with the utmost wisdom. Yet the opinions of students of the question and the success of modest efforts already made are united in encouraging us to hope that something may be accomplished by this form of education in the future. The conventional objection, of course, is that the industry of prostitution is regulated by the law of supply and demand and that it cannot, therefore, be influenced by an educational campaign similar to that being made against other diseases. But it is common experience that demand may be contracted or expanded almost at will; it is daily increased by advertisement and frequently diminished by boycott. In the case of prostitution there seems to be no reason for doubting that the more reasonable portion of the youth of a land could be, to a degree at least, protected against its dangers by a thorough understanding of those dangers. For it must be remembered that syphilis is most frequently contracted during the years of inexperience. By an examination of 11,000 cases Edmond Fournier has shown that the maximum incidence is attained at the twenty-third year in men and the twentieth year in women. There is no question that the medical profession should stand behind any wisely considered attempts to give to the youth of the land the instruction which they fail to get at home; and in this movement no one can accomplish more than the general practitioner. For if the source of syphilis is ever to be rendered relatively innocuous it

will only be done by making the public understand what a menace to health prostitution really is.

(*c*) It is immediately incumbent on the medical profession to keep itself informed and to instruct the public as to the danger of innocent syphilitic contagion. Nothing can be more tragic than the disease acquired in this way, and in a large number of instances information and reasonable care would have entirely prevented it. The danger of transmission by wet-nurses and by many of the contacts of every-day life should be known to all men.

(*d*) The close association between alcoholic abuse and the contraction of venereal disease being an absolutely established fact should, in the interest of public health, be more widely appreciated. "Sine Baccho friget Venus;" "Der schlimmste Kuppler ist eben der Alkohol;" "Aus der zwei V, Vinum und Venus, entsteht ein grosses W (Weh)." The simple fact behind these popular statements gives the physician sufficient warrant for regarding the alcohol problem as a distinctly hygienic problem quite from the standpoint of the syphilographer.

(*e*) Lastly must be mentioned the close association between the prophylaxis of syphilis and many social reforms. This is not the place to go into these matters in any great detail; but there can be no doubt that public hygiene demands attention to them on the part of medical men. Prostitution, the great source of the disease, is at present a part of the social fabric; and it exists, partly at least, because of the injustices of society. No movement therefore which makes for improved industrial and hygienic conditions can fail to be of service in the fight against syphilis. Neither bathos on the one hand nor smug Pharisaism on the other is the attitude to take toward the source of this plague. And the questions of female pauperism, of improved tenement quarters, of proper female education, of wholesome amusements for the poor—these are problems which, although properly sociological, have a distinct medical interest and importance.

4. **The Private Hygiene of Syphilis.**—There can be little doubt that the physician has a distinct duty to fulfil to his patients in explaining to them certain elementary hygienic details which cannot well be publicly considered, and which do not enter into the prophylactic campaign of the State. There is first the question of continence, and here the physician dare teach his patients but one thing, namely, that continence, no matter how difficult, is the relation of greatest safety for the individual and for society and is not detrimental to health.

As to the more immediate measures of private hygiene, the physician has little to do that has not already been mentioned. It certainly is not part of his function to sacrifice his professional dignity to the extent of advising certain protective measures for rendering illicit intercourse safe. For the health of the commonwealth must be one of his considerations as well as the health of a single patient; and quite aside from the value of this or that measure, or the fact, for instance, that the famous mot of Ricord about the most common form of protection is as false as it is sententious, this is a business in which the physician with any sense at all of his moral obligations can have no hand, provided he has, as he *should* have, a proper sense of the danger to public health of illicit intercourse.

**The Prophylaxis of Hereditary Syphilis.**—This is the most tragic form of the disease; and it is therefore unusually satisfying to know that much can be done toward preventing it. The most certain prophylaxis consists, of

course, in proper treatment of the parents before marriage. In statistics compiled by Fournier, it has been shown that the infantile mortality of the issue of subjects whose syphilis has been properly treated is only about 3 per cent. In 45 pregnancies, however, occurring after the marriage of untreated syphilitics, the mortality was 82 per cent.

We are here concerned rather with the question as to whether there is any hope of protecting the fœtus by treating a healthy mother who has conceived by a syphilitic man. It has been shown that mercury and potassium iodide pass from mother to child through the placenta. Porak demonstrated iodide in the urine of a fœtus forty minutes after its administration to the mother; Cathelineau and Stef found mercury in the bodies of fœtuses whose mothers had received it. This sort of prophylactic treatment is therefore rational, and, as a matter of fact, it has producted excellent results. Women, for instance, whose previous pregnancies had been disastrous, have frequently had normal pregnancies when specific treatment was instituted; and the following rule may be formulated: "When a woman is pregnant with a child threatened, by paternal antecedents, with syphilitic heredity, syphilitic treatment of the mother, although healthy, constitutes for this child a real and powerful safeguard for which there is a precise and formal indication."

Treatment to be effective must be begun in time. "After the fifth month it is too late," says Pinard. Mercury is the drug to be given, and is best administered in the form of the proto-iodide pills. The fœtal dose cannot, of course, be accurately guaged, but about gr. ½ is usually a sufficient dose. The treatment should be continued during the whole pregnancy. Pinard advises continuous treatment, but others prefer the intermittent method—twenty days' treatment and ten days' rest every month.

**Treatment.**—I. **Initial Stage.**[1]—It is usually the appearance of the chancre which brings syphilitic patients for treatment. In many instances, it is true, the chancre is entirely overlooked or neglected and the patients are first seen with secondary or tertiary symptoms; but as a rule the physician's therapeutic problems begin with the chancre itself. And the questions with which he must concern himself are the two following: (*a*) How should the chancre itself be treated? (*b*) When should constitutional treatment be started? The idea that the primary sore is a local affection, and that syphilis might therefore be extinguished *ab ovo* by treatment directed at its primary manifestation has always been an attractive one. In 1514, Jean de Vigo advised it and Hunter believed in it thoroughly. Several methods of accomplishing the purpose have been suggested.

(*a*) *Blockading the Chancre.*—Mercurial injections about the lesion, injection or excision of the neighboring glands, and even division of all the lymphatics (!) have been proposed.

*Cauterization* of the chancre has, however, been a more feasible and a more widely used procedure. Chemical caustics (Ricord's carbosulphuric paste, Vienna paste, etc.), the actual cautery, and specific caustics (a substance being used which is both caustic and an antidote to the syphilitic virus) have all had clinical application.

*Excision* of the chancre was a popular therapeutic procedure in the early history of syphilis, but fell into disrepute on account of its failures. In 1877,

[1] Fournier's incomparable *Treatment of Syphilis and Prophylaxis of Syphilis* are now published in English translation (Rebman Co., 1906). Nothing better exists on these subjects.

however, Auspitz again drew attention to it and since that time it has received a good deal of notice. The procedure is simple, provided the lesion be situated on a part which can be resected without damage; chancres of the meatus, however (for example), could hardly be treated in this way. It is essential that a margin of healthy tissue about the lesion be removed with it, and to avoid contamination of the wound the chancre itself should first be destroyed with the thermocautery. The wound usually heals quickly, with a small scar. In excision of chancre of the penis, hemorrhage is sometimes severe. Recurrence of the lesion *in situ* is not uncommon, and a third induration may even occur after excision of a second one.

In spite of the attractiveness of these various methods of attacking the primary sore the procedure has led to doubtful if not wholly disappointing results. It is irrational because the chancre, so far from being the source of the disease, is but an early expression of it; and to expect that its ablation will cure the disease would be like treating typhoid fever by excising a rose spot. It is further irrational because experimental work has shown its uselessness. In the experiments of Neisser carried out in Java, injections of sublimate begun immediately after the inoculation of the syphilitic virus prevented neither the development of a chancre nor the general distribution of the virus throughout the body. But it is the clinical failure of the method that is most important. Cauterization of a chancre, even in its earliest stage, is absolutely powerless to prevent constitutional infection. Langston Parker cauterized a chancre of two hours' duration without preventing constitutional symptoms; Berkeley Hill cauterized a ruptured frænum with fuming nitric acid eleven hours after a suspicious intercourse, but the wound became indurated and secondary symptoms followed. Many other similar experiences are recorded. Specific cauterization, widely used by Hallopeau, has given no better results.

Excision has had, and still has, enthusiastic advocates; but there is no question that its failures far exceed its successes. Furthermore, even its successes are of a doubtful nature; for in view of the great difficulty in the diagnosis of an early chancre there is always the suspicion that the sore excised was chancroidal and not luetic. In a certain number of instances there is little doubt that this was the case. In nearly all cases where the attempt has been made to establish the probability of syphilis by confrontation, excision has failed. It has even failed when done during the first few hours of the chancre; cases in which excision was practised twelve hours after the appearance of the chancre are reported by Rasori and by Taylor, and one in which the chancre was ten hours old by Brandes. In all, constitutional syphilis developed. Ricord went so far as to say: "Even if we amputated the penis as soon as the chancre appeared, syphilis would none the less certainly follow." Ablation of skin of the penis where a chancre *would be likely to appear* has even been practised after suspicious intercourse and before any signs of a chancre were present; but infection was not prevented and general syphilis occurred without a chancre. Furthermore, excision of the primary lesion has not succeeded in even attenuating the subsequent constitutional syphilis.

The treatment of the chancre, therefore, consists in doing nothing. This is particularly important if there is any doubt about the diagnosis; for cauterization of the sore will destroy its normal appearance, prevent its normal evolution, and thus make the diagnosis further impossible before the appearance of constitutional symptoms. In these cases simple cleanliness and

dusting with calomel powder suffice. When the diagnosis of the sore is quite certain, excision may be practised to get rid of a none too pleasant lesion and to ease the patient's mind. No other results should be expected of it, although it is still within the realms of possibility that it may do good. Now that Schaudinn's discovery has made early diagnosis of the sore possible, the whole subject needs further experimental study. Extensive cauterization cannot be too heartily condemned; tampering with powerful caustics may turn relatively benign chancres into deforming phagedenic lesions which promptly heal when kept clean and let alone.

(*b*) When should constitutional treatment be begun? Briefly, it should be begun the moment a positive diagnosis of syphilis can be made. The disease should be attacked too soon rather than too late; for when treated from its commencement it generally shows itself amenable to treatment, benign in its symptoms, and relatively less severe as regards later manifestations. On the whole, syphilis is more dangerous and less curable when treatment is begun late; early treatment often prevents many of the distressing and compromising secondary symptoms, and, if the diagnosis be made, "it is impossible," in the words of Hutchinson, "to commence too soon." But *only, if the diagnosis be made;* for in cases where careful and minute examination of the lesion leave one in doubt as to its nature it is better to wait until the appearance of confirmatory constitutional symptoms before prescribing mercury. Unfortunately, a large proportion of the cases are of this kind; for anyone who has seen many venereal lesions will appreciate the very great difficulty of making a positive diagnosis on the appearance of the sore alone. It is just here that examination for the presence of the organism of Schaudinn is of the greatest value; for if the spirochæte be found, we are justified in regarding the lesion as luetic and in immediately instituting treatment. In cases, however, where doubt still exists as to the nature of the sore, we must wait for secondary symptoms, and for the following reasons:

(1) We lose little by this procedure. We need wait, at longest, only a few weeks; and as the disease is already constitutional when the chancre appears, we are not permitting a local infection to become a general one, but a general infection to express itself constitutionally.

(2) The efficient treatment of syphilis is no light matter. It is never agreeable, often disturbs the general health, and must last over a period of two years at the very least. For these reasons the best results are only obtained with intelligent patients; they are *never easily* obtained; and the absolute conviction of both patient and physician that a serious affection is present is essential. But if early treatment be instituted before a positive diagnosis is made, the secondary symptoms may be obscured, no certainty will ever exist, and treatment will surely be lax.

(3) It is of the highest importance for a man to know whether he has syphilis or not. "A disease," said Ricord, "which grips forever the body of its victim, a diathesis which pursues its victim all his life, and beyond it to posterity, a constitutional taint, transmissible and hereditary—these are not vain and frivolous considerations." They are considerations, indeed, which a man should face in the most intelligent manner possible; but they cannot be intelligently faced if treatment "at all hazards," mercury "prescribed for the sake of prudence," have obscured the diagnosis from the start. For a diagnosis thus obscured may remain obscure; and a patient may suffer from late effects of the disease which properly continued treatment would

have prevented. The situation is particularly embarrassing when the question of marriage comes up. "If the patient has had syphilis," writes Fournier, "a few months' treatment will not prevent his being dangerous for his wife and future children. But if he has not had syphilis, why should be he condemned to celibacy? There is no escape from this situation; it is a blind alley."

II. **The Secondary Stage.**—With the onset of constitutional symptoms and the establishment of the diagnosis, treatment becomes as active as it had been inactive during the primary stage. The physician now has a patient whose general health must be watched and provided for, and whose specific disease must be vigorously attacked.

1. *The Auxiliary Treatment.*—Syphilis is not completely treated by the simple prescription of mercury or potassium iodide. It is true that in many cases this suffices; but in certain patients, more particularly in nervous women, auxiliary treatment is of very great importance.

(*a*) *Diet.*—Many idle words have been written as to the syphilitic diet; and although the matter is by no means unimportant, it is quite simple and to be summed up in a few words. The keynote is the avoidance of excess. Irregularities of diet are to be forbidden and food and drink which cause diarrhœa or are prejudicial to the gastro-intestinal functions are to be avoided. Alcoholic excess is particularly dangerous. With these exceptions the diet should be interfered with as little as possible.

(*b*) *Hygiene.*—Here again avoidance of excess is the keynote. Overstimulation of an organ directs the syphilitic virus to that organ. Cerebral syphilis, for example, is especially common after nervous and intellectual overwork, after excitement, dissipation, and venereal or other excesses. Again, buccal syphilides are most frequent and more serious in tobacco users. For these reasons one should insist on the very great danger of overstrain to a syphilitic under treatment, and forbid tobacco.

Not an unimportant part of the physician's hygienic duty to his patient consists in attention to his state of mind. "Avoid sad passions" was the old advice to syphilitics; but, as Diday said, "Of all the anguishes, it is often the syphilitic anguish which lies heaviest on the syphilitic." This is the sad passion which the physician should correct. He can, fortunately, tell his patient, with truth, that the disease is curable, that safe marriage is possible, and that the prospect for healthy posterity is good. This wholly warranted assurance may be a very vital part of the treatment of the disease.

(*c*) Special attention must be paid to patients with *nervous predispositions.* It is the nervous system which is most often attacked by tertiary syphilis, and to these dangers nervous patients are more liable than others. It is the hereditarily neuropathic patients and the patients subject to nervous overwork who are especially subject to these calamities. Neurasthenia may be called one of the "localizing causes" of syphilis, and neurasthenic patients should be particularly careful in the avoidance of excess of every kind. Hydrotherapy and other more specifically neurasthenic treatment should also be used.

2. *The Specific Treatment.*—For all practical purposes the specific treatment consists, in the administration of mercury and iodide, either separately or in combination. A whole host of other drugs have been used, and some of them have been championed with enthusiasm. None has shown, however, any true antiluetic property; and except for more or less important adjuvant value, none possesses more than historic interest.

(*a*) *Mercury.*—This drug has now been shown by extensive clinical application to possess a power over syphilis, at least in its secondary stage, that has almost no parallel in medicine. This power is in direct proportion to the amount of the drug taken up by the economy. The drug is, at the same time, not without its injurious effects, and cannot be recklessly given. In the effort therefore to combine the maximum of therapeutic effect with the minimum of untoward symptoms, several methods of mercurial administration have come into use.

(1) *Ingestion.*—This is the method most widely used, not because it is free from disadvantages, but because it is practical, in the sense that it is easy, convenient, and efficient. Nearly all the preparations of mercury known to chemistry have been administered by the mouth. Metallic mercury, calomel, the biniodide, the binoxide, the black sulphide, the acetate, the cyanide, the so-called peptonate and tannate, and the salicylate of mercury have been tried; but it is the proto-iodide and the bichloride which have, after long experience, proven themselves most valuable.

Proto-iodide is insoluble and can therefore only be administered in the form of pills. The dose varies from gr. $\frac{1}{6}$ to gr. j (0.01 to 0.06 gm.). A small dose of opium, gr. $\frac{1}{3}$ (gm. 0.02), is often prescribed with the mercury to prevent gastric irritation, the most famous combination of this sort being Ricord's pill.[1]

Bichloride of mercury may be given either in pills or in solution. The usual dose for an adult is gr. $\frac{1}{16}$ (gm. 0.004) three times a day. This, too, is often combined with opium, to assure gastric tolerance for the sublimate, as in the well-known Dupuytren's pills, but the drug is preferably given without opium in pill form or in solution with a small amount of gum acacia. Sublimate solution is irritating to the stomach and should be given in a dilute form. On account of its objectionable taste and also to diminish gastric symptoms, syrup of sarsaparilla or peppermint may be prescribed with it. If taken in milk the drug is also found better tolerated by the stomach.

Gray powder (mercury with chalk) is a form of mercury particularly lauded by certain authors. It may be given in gr. $\frac{1}{2}$ (0.03 gm.) doses, and is Hutchinson's favorite form of treatment. In cases of visceral disease with ascites the well-known Addison's pill (containing calomel, digitalis, and squills) is useful; but in general the visceral lesions (more particularly syphilitic hepatitis) require in addition the administration of iodides. Bichloride of mercury is also frequently prescribed in combination with potassium iodide.

The mercurials administered by the mouth may also be given per rectum in the form of suppositories. This method of administration is mentioned for the sake of completeness, rather than because it possesses any unique advantages.

(2) *Inunction.*—This is the oldest of all the methods of administration of mercury. It consists in anointing the skin with salves containing the drug in a suitable form and in the olden days included, among other things, as

[1] The original formula of Ricord was as follows:

| | |
|---|---|
| Proto-iodide of mercury | 3 grams. |
| Extract of thebaine | 1 gram. |
| Thridace | 3 grams. |
| Confection of roses | 6 grams. |

For sixty pills

an important part of the treatment, depuration by purgatives and by bleeding. The ointment most often used is the well-known blue ointment, composed of equal parts of mercury and lard (double mercurial ointment, Neapolitan ointment). Lanolin may be substituted for the lard and is said to penetrate the skin better. Mercurial soaps have also been used, but, in spite of certain advantages, have not replaced the blue ointment. Mercury-vasogen (which may be had in 33 per cent., 50 per cent., and 75 per cent. mixtures, and should be ordered put up in gelatin capsules containing the required dose) is a very clean and efficient form of ointment for this purpose, and in private practice should always be prescribed. Its expense is its only disadvantage. The average dose of mercurial ointment is 1 dram. For women, who are more subject to salivation from inunctions than men, ½ dram is, as a rule, a sufficient dose. Infants tolerate inunctions well and proportionally larger doses may be prescribed for them; in quite young infants 15 to 30 grains may be safely used. The inunctions should be carried out to the point of dryness; for a dose of 1 dram this requires at least 30 minutes. One inunction is usually prescribed per day for six days of the week; it is omitted on the seventh day, when a hot bath, preferably a Turkish bath, or a sweat bath is taken. The hairy regions of the body should be avoided in applying the ointment, as inunctions in these regions lead frequently and rapidly to stomatitis and often cause dermatitis. To avoid mechanical irritation, the seat of the inunctions should be varied, the sides of the thorax and the inner surfaces of the thighs and arms being chosen.

The inunctions are best given at night before retiring, the site of the application being covered with cotton, after rubbing, to prevent soiling and to keep the ointment from being wiped away. The inunction treatment is quite efficacious even when simply carried out; but a regular sweating bath[1] is beyond doubt of advantage, and life at a mineral spring, where hydrotherapy is assiduously practised, large amounts of water drunk, and frequent Turkish baths taken, makes it possible for the patient to absorb larger amounts of mercury than can be taken up without such auxiliary treatment. The inunction treatment should be interrupted from time to time and a recess of a few days taken to avoid stomatitis, and the mouth, in all cases, should be very carefully watched during the treatment.

(3) *Injection.*—The introduction of mercurials under the skin was originated by Hebra and Hunter, but it was first widely used after the publications of Lewin in 1867. The technique of the procedure is quite simple. The injections are best made into the buttocks, well above the ischial tuberosities, the two buttocks being used for alternating doses. An all-glass syringe is the best to use; the needle should be of sufficiently large caliber, and it is essential that it should be long enough to reach well through the skin and subcutaneous fat. For the injections, although often spoken of as hypodermic, are, or should be, intramuscular. The skin is washed with green soap and water and swabbed with ether. The needle is then plunged straight into the muscles, and watched for a moment to see that no blood escapes. If blood *does* escape, the needle should be re-inserted. The syringe is then attached and the injection made. When the needle is withdrawn, a small collodion and cotton dressing over the puncture wound is sufficient.

[1] Vapor baths may now be purchased quite cheaply and these may be used by patients in their homes.

Both soluble and insoluble forms of mercury have been used for this purpose. Of the former, bichloride and biniodide; of the latter, metallic mercury, calomel, and salicylate of mercury have been the ones most frequently employed. The following are the formulæ:

*Bichloride.*—

| | |
|---|---|
| Hydrarg. chlor. corros. | gr. j. |
| Glycerini | ʒij. |
| Aquæ destillat | ʒij. |

Sig.—Injections of ♏v to xv every one, two, or three days.

*Biniodide.*—This may be given in a 0.4 per cent. solution in olive oil. The injections may be given every day, the dose at the start being ♏x, which is rapidly increased to ♏xxx or even ♏l.

*Metallic Mercury.*—This is given as the gray oil, introduced by Lang, of Vienna. Half an ounce of mercury is rubbed up with 2 ounces of anhydrous lanolin, and the mixture then increased to 5 ounces by the addition of paraffin oil. Enough carbolic acid should then be added to make a 2 per cent. solution for antiseptic purposes.[1] This mixture should not be warmed, in which case the mercury separates out; nor cooled, in which case the solution stiffens. The dose is ♏x and the injections may be given once a week or once every five days.

| | |
|---|---|
| Calomel | gr. xxiv. |
| Glycerin | ʒij. |
| Distilled water | ʒij. |

This may be sterilized by placing the bottle in which it is kept in boiling water and keeping it there for an hour. The dose is ♏v to xv (gr. $\frac{1}{2}$ to $1\frac{1}{2}$) injected every five to fifteen days. Olive oil, oil of vaselin, oil of almonds, and distilled water may also be used for making the suspension.

*Salicylate of Mercury.*—This is best given as a 10 per cent. solution in liquid albolene, which may be sterilized by heating. The dose is ♏x once or twice a week. The injections usually cause no local disturbances, but indolent nodosities have been seen after the use of salicylate.

Certain authors have also advised the use of massive doses of soluble salts of mercury. This is dangerous; for the rapid absorption, which is quite beyond one's control, may lead to alarming symptoms. Moreover, although intense mercurialization may be thus produced it does not appear that the influence of such injections on the disease is a persistent one.

Intravenous injection of mercurials, introduced by Bacelli, of Rome, has, in spite of its dangers, found certain staunch supporters. Bacelli used bichloride in 0.1 to 0.2 per cent. solutions, 1 cc. (representing gr. $\frac{1}{64}$ to gr. $\frac{1}{32}$), being injected. The therapeutic effects have not, however, been superior to those of other methods. Lang has suggested paravenous injections for the purpose of having the mercury reach the blood promptly, but not too directly.

(4) *Fumigation.*—This, too, is quite an old method of treatment. Like inunction, it formerly included sweating and depuration. Previous to the invention of the fumigation box by Lalouette in 1776, the patient was entirely enclosed in a chamber in which mercurial vapors circulated; and inhalation of these vapors caused dangerous symptoms and even fatalities.

[1] This is the principle, although not the exact formula, of Lang. The formula is the one recommended by Lambkin, of the British army.

Nowadays the patient, seated, is covered up to the neck by a sheet which reaches to the floor. Under the chair is placed a voporizing apparatus containing 15 to 60 grains of calomel. The calomel is volatilized and the patient is bathed by the vapors. Volatilization is usually complete in fifteen minutes, after which the patient is left for another ten minutes in the vapor. He is then put to bed for forty-five minutes, wrapped in the same coverings. The treatment may be repeated every day or used only twice a week.

(5) *Mercurial Baths.*—This method of treatment, formerly much in vogue, particularly in infantile syphilis, is now little used. A series of baths is given to which the following solution of mercury is added:

| | | |
|---|---|---|
| Bichloride of mercury<br>Hydrochlorate of ammonia . . . . . | āā | ʒv. |
| Water . . . . . | | ʒvj. |

(6) *Mercurial Plasters.*—These, formerly much lauded, have fallen into disuse. The famous *emplastrum* of Vigo, contained besides mercury twenty-three other drugs, each possessing marvellous qualities; but the plaster now used is the sparadrop of Quinquad, who has studied the subject scientifically:

| | |
|---|---|
| Diachylon plaster . . . . . | 30 parts. |
| Calomel . . . . . | 10 parts. |
| Castor oil . . . . . | 3 parts. |

This is applied to the skin for a week and then renewed until the desired effect is produced.

*Merits of the Various Methods of Mercurial Administration.*—Fumigation, treatment by mercurial baths, and treatment by plasters have, except in rare instances, little that can be said for them. Of the other three methods—inunction, ingestion, and injection—it is difficult to say dogmatically that any one is always and everywhere the best. "There should be nothing absolute in the choice of a therapeutic method," says Fournier; "this choice should always be subordinated to individual indications; indications concerning the patient and the disease; indications which are naturally of the most varied nature." The advantages and disadvantages which inhere in each must, however, be known in order that intelligent choice of method may be made.

Ingestion is particularly appealing by reason of its ideal simplicity. It is less liable than inunction to cause stomatitis, and the stomatitis which it causes is of a less rapid and severe type. It avoids the pain and occasional accidents of injection. The method is, on the average, best suited to the occupations, convenience, and social and professional obligations of the average patient; and the probability that convenience of form of treatment will make for prolonged and efficient treatment is not to be lost sight of. Patients who will not submit to inunctions or return for injections will swallow pills almost indefinitely; and for these, and other reasons, the method of ingestion remains the method of choice for the average patient. It must not be forgotten, however, that the method has the disadvantage of leaving the treatment largely in the hands of the patient. It is contra-indicated when the digestion is poor, or when experience shows the stomach to be intolerant for the drug; when the patient is cachectic and must have his digestive powers respected; when the digestive organs must be left free for other remedies which may be required; and when a pressing and urgent danger renders rapid mercurialization necessary. Ingestion can, however,

as will be shown later, be quite well combined with inunction or injection. The chief advantage of inunction is its active therapeutic effect. This may be an absolute indication for the choice of this method where urgent symptoms are present. But the absence of gastric complications is an additional advantage. Again, inunction leaves the stomach free for other medication; either the exhibition of iodides, when mixed treatment is carried out or the administration of auxiliary medication (potassium bromide, tonics, etc.). On the other hand, it is a dirty, inconvenient, and repulsive method, involves a certain amount of publicity, and often discourages patients, leading them to abandon treatment altogether. It is occasionally accompanied by diarrhœa and by dermatitis; and quite commonly by stomatitis which occurs more frequently with this method than with any other. Moreover, the stomatitis which it causes is more rapid in its onset, more general and more intense in its manifestations, than that seen after ingestion. Inunctions are also somewhat uncertain in their effects; one patient responds well to them, another badly. This is no doubt due to the way in which the rubbing is done, and for this reason the method is not always applicable. It cannot be too strongly insisted that patients who are receiving inunctions should be carefully watched, particularly as to the development of stomatitis; and that care should be taken that the rubbing is well done. The method is indicated in severe cases (cerebral and spinal syphilis), in cases refractory to other methods, in dyspeptics and those subject to diarrhœa, and in cachectic patients. It is of particular value in the treatment of syphilis in young infants, whose lives may depend on the integrity of the digestive system.

The method of hypodermic injection is a relatively accurate one. The drug must be administered by the physician, and deceit as to the amount of the drug taken is therefore avoided. The chief advantage of the method is its therapeutic intensity; it induces mercurialization rapidly and intensely, and is of particular value in the presence of urgent symptoms. It also leaves the stomach free for other medication, and does not, as a rule, cause intestinal symptoms. It is claimed that the hypodermic method ensures the most exact dosage of mercury; but this accuracy is an apparent rather than a real one; for the sufficient dose of a drug is to be estimated not alone by the amount given, but by the physiological effects obtained, and these can be estimated quite as well when inunctions or ingestion are used. Pain and local irritation are strong objections to the method; for, aside from the inconvenience caused, these are often sufficient to drive the patients away and make them neglect treatment altogether. The formation of nodosities and sloughs is occasionally seen, although only occasionally with present-day technique. The method is, on the whole, not practicable because it requires an amount of attention on the part of the patient which the patient does not, as a rule, feel willing to give. It is not wholly free from danger. Several cases of pulmonary embolism have been reported following the subcutaneous injection of calomel; and hemorrhage and nervous accidents (partial paralysis, trophic disorders, etc.), although rare, have occurred. The method is one of "special indications."

Intravenous injections may be given quite without pain. Local accidents are, as a rule, absent; the dose given is mathematically controlled; and much has been claimed, by enthusiasts, for the therapeutic results. As a rule, however, it has been pretty generally abandoned, and is now recommended only when very rapid action is required. The technique is not altogether

simple, as the vein may be missed; and local accidents, although not frequent, do occur. Moreover, the therapeutic effects of the method have not been encouraging, and most authorities hesitate to advise such sudden introduction of a toxic substance directly into the blood stream.

*The Disadvantages of Mercury.*—Aside from the question of method of administration, the dangers of the drug itself must be considered. Stomatitis is the complication most frequently seen. This was formerly regarded as an essential part of the cure; in the days of Astruc "a good cure required a good salivation of 4 or 5 pounds a day." The stomatitis now observed, however, is usually of a milder type and begins as a gingivitis. The saliva becomes stringy and superabundant; there is a metallic taste in the mouth; the gums (especially of the lower jaw) become reddened and swollen and bleed easily; the teeth become tender and appear to the patient to be elongated. There is a metallic and fœtid odor to the breath. In bad cases, now not often seen, the entire mucous membrane of the mouth is swollen, ulcerated, and bleeding; ropy saliva wells from the lips; the teeth are exceedingly tender, become loose, and may even fall out. The ulcerations of the buccal mucosa may resemble mucous patches quite closely. Stomatitis may often be prevented by prophylactic measures, including: (*a*) Choice of remedy and method of administration; ingestion is less frequently accompanied by stomatitis than injection or inunction, and proto-iodide more frequently than sublimate. (*b*) Hygiene of the mouth. Neglected mouths are particularly subject to stomatitis, and mercury should never be given without inspection of the mouth. Where this is in bad condition, attention should be paid to it. But in any case the teeth should be carefully and regularly brushed and the mouth frequently washed with a solution of chlorate of potash or some astringent wash. The gums may be occasionally painted with tincture of iodine. Patients should also be informed of the buccal accidents of mercury and told to report immediately if any symptoms are noticed. On the least sign of buccal irritation, mercurial treatment should be discontinued.

Salivation, when present, is treated, as follows: Stop mercurial treatment and order immediate and repeated Turkish or vapor baths. See that the bowels are kept open and that large amounts of water are taken to stimulate the kidneys. Order a potassium chlorate or potassium permanganate mouth wash to be used every hour, and internal doses of potassium chlorate (5 grains three times a day) for three or four days. Atropine in doses of gr. $\frac{1}{32}$ (0.002 gm.) may be given. The gums may be painted with the following solution:

| | | |
|---|---|---|
| Tinct. krameriæ, | | |
| Tinct. iodi . . . . . | āā | ℥v. |
| Tinct. myrrh. . . . . | | ℥iiss. |

In ulcerous stomatitis hydrobromic acid or silver nitrate should be used to cauterize the ulcers.

Gastro-intestinal complications are not infrequent during mercurial treatment. These may take the form of pains in the stomach, colic, diarrhœa, loss of appetite, or even persisting dyspepsia. Some corrective (such as opium) will often suffice to prevent or attenuate these complications. But even the strongest stomach may become fatigued by the remedy, and treatment should therefore be now and then suspended, to give the digestion a respite.

Disturbances of nutrition, in the form of languor, anæmia, want of appetite, fatigue, and emaciation, occasionally occur, particularly when mercury has been too strenuously prescribed. The nutritional dangers of mercury have, however, been exaggerated; their occasional occurrence is but one more argument for the careful and intermittent administration of the drug.

*Cutaneous Complications.*—Irritative dermatitis from inunctions is a local affair and may, by varying the site of inunction, be avoided. The absorption of mercury also causes eruptions. They are due to a personal idiosyncrasy and occur with even very small doses. The most common form is that of desquamative polymorphous erythema. In the milder cases, the symptoms consist only in local heat and itching, with slight fever. Occasional cases are severe, the clinical picture being that of a severe, extensive burn.

Other manifestations of hydrargyrosis are albuminuria, cylindruria, and changes in the nervous system (particularly polyneuritis).

(*b*) *Potassium Iodide.*—This drug, introduced into the treatment of lues by Wallace and popularized by Ricord, takes the place in the therapeutics of the tertiary stage which mercury holds in that of the secondary. It is very soluble in water, rapidly absorbed, and appears in the urine twenty minutes after ingestion. The economy soon becomes impregnated by it and it may be found in all the secretions. Its antisyphilitic power is quite miraculous and its power to dissolve luetic tumors is the most dramatic thing in therapeutics. The drug may be administered by the mouth, by the rectum, or hypodermically; but inasmuch as it is usually well tolerated by the stomach, the second two methods have little more than theoretical interest. In certain rare cases the administration by enemata might be indicated, as in unconscious patients in whom it was not desirable to pass a stomach tube; but for all practical purposes the drug should always be administered by the mouth. It should be given in weak solution, as strong solutions have a disagreeable taste and irritate the stomach. The taste may be masked by giving the drug in milk or wine or by adding peppermint or one of the syrups (the best is syrup of bitter orange). In cases where the taste of iodide is persistently nauseating, one has to experiment until some pleasant drink is found which successfully masks it. The drug should be taken after or during meals. In some patients it causes constipation, in others diarrhœa; and a mild purgative or astringent should in these cases be prescribed with it. It may be ordered in the saturated solution, the required number of drops being put into the milk or other drink which is to be used.

As to the dosage, there is divergence of opinion. Some advocate small, others extremely large, doses. Fournier thinks that the method of beginning with small doses is bad, for it is the small doses which appear to be particularly harmful. On the other hand, he is strongly against what he calls "iodide debauches." He begins, for an adult man, with 30 grains daily (given in three doses); for a woman, with 15 to 20 grains. The dose is gradually increased until it reaches 45 to 60 grains daily, and here it remains. When the indications are very urgent larger doses (beginning with 70 to 90 grains and rapidly increasing to 150 to 180) are given; but doses of 500 grains he considers useless "intemperance." When tolerance for the drug is established, the curative value apparently diminishes, and the dose must therefore be increased. Other authors, however, advise larger doses, beginning with

30 to 40 grains daily and increasing a grain a day until about 250 grains daily are given. Gottheil reports a case of gumma of the meninges which only showed improvement when 900 grains were administered daily; half of this was introduced into the stomach through a tube and the rest into the rectum in enemata. Whether parasyphilitic affections would be prevented by routine employment of massive doses, as claimed by some authors, is a point still unsettled.

Iodide of sodium, ammonium, and rubidium, iodine, iodoform, and other iodine compounds have been used instead of iodide of potassium; but none of these has yet proven itself a satisfactory substitute.

*Iodism.*—Potassium iodide, like mercury, joins with its remarkable therapeutic value certain untoward effects. The cause of these symptoms seems to be an idiosyncrasy in the patient. They appear after small doses and often early in the treatment. The most common are the iodic taste, coryza, and acne. The taste is a slightly salty or metallic one, is especially noticed in the morning, and is most frequent in women. The coryza is much like that of an ordinary cold in the head; it is characterized by snuffling, a sense of nasal obstruction, running from the nose, frontal headache, etc. The discharge from the nose is usually serous. The coryza may disappear in a few hours or last, in a subacute stage, throughout the treatment. The acne eruption generally appears on the face in the form of recurring crops of acneform pustules, seldom more than four or five at a time. Both the coryza and the acne may appear in severe form, the former resembling influenza (iodic grippe) and the latter appearing as a large, furunculoid, deforming eruption. Other rarer symptoms of iodism are neuralgic pains, especially of the jaws, and most often seen in women; a mild sialorrhœa, never so intense as in mercurial salivation; conjunctivitis; iodic purpura; gastro-intestinal symptoms (nausea, vomiting, diarrhœa); swelling of salivary and parotid glands (iodic mumps); and localized œdema, especially of the eyelids.

The eruptions of iodism, which are sometimes severe and occasionally fatal, appear in three general types: the bullous type (iodic pemphigus), the furunculo-carbuncular type, and the pustulo-crustaceous type. The latter may be impossible to distinguish from tertiary syphilides; the rapidity of invasion, the initial form of the eruption, the inflammatory character of the areola, the soft base, and the disappearance of the eruption on suppression of the drug make the diagnosis. Purpura may occur. Iodic œdema of the respiratory passages, sometimes requiring tracheotomy and occasionally ending in death, is another rare symptom of iodism which must be mentioned.

The accidents of iodism are not as a rule severe; the symptoms often disappear as tolerance is established, and suppression of the drug is not necessary. When they do not disappear, it may be discontinued for a short period. For patients who are subject to localized œdema and to prevent the nasopharyngeal accidents, belladonna may be exhibited, 1 grain of the extract being given daily.

*Mixed Treatment.*—It is true that mercury is the drug, *par excellence*, which is indicated, roughly, in the early stages of syphilis; and that the iodides produce their most remarkable effects in the later stages of the disease. Syphilis, however, may be entirely cured without the use of iodides, the administration of which in lues is only a matter of relatively recent years. Furthermore, iodides have, as a rule, only a slight influence on the secondary phenomena. They are not, therefore, in any sense of the word a substitute

for mercury. To say these things, however, is by no means to warrant us in dividing syphilis into two halves, for one of which mercury and for the other iodide is indicated; for iodide may be of use in the secondary stage and mercury is an antisyphilitic at every period of the disease.

In the secondary period iodide has a marked influence on the headaches and should be prescribed in 15 grain (1 gm.) daily doses. It is also of value for the vague neuralgic pains which are especially common in women. In early malignant syphilis—which is really tertiary syphilis succeeding the chancre without a secondary stage—iodides are of benefit; and they are indicated whenever mercury cannot be tolerated by the patient in any form. Mercury, on the other hand, seems to be always useful as an auxiliary agent in the tertiary stage; it may, indeed, even replace iodides, certain of the lesions (notably sarcocele), which had failed to yield to iodides, having been cured by mercury. Moreover, it must be remembered that it is mercury which cures syphilis; iodide "erases the symptoms." "As a preventive medication," therefore, "there is much more confidence to be placed in mercury than in iodide."

For these reasons the method of mixed treatment is the one that should be followed. The drugs may be administered separately or together. The best plan is to order a solution of iodide in syrup to be taken at the same time as the mercury; or to prescribe mercury by inunctions and potassium iodide by the mouth. A very satisfactory plan is to combine the exhibition of potassium iodide with mercurial injections.

**Treatment of the Local Manifestations.**—1. *The Chancre.*—The treatment of the chancre has been discussed above.

2. *The Syphiloderms.*—These, as a rule, require no attention. When on the face or hands they may be made to disappear more rapidly by the use of white precipitate ointment. The tuberculous and pustular syphilides require more energetic treatment; white precipitate ointment may be used, or a 10 to 20 per cent. solution of the oleate of mercury in oleic acid. For the alopecia, local inunctions of blue ointment are advised.

3. *Mucous Patches.*—Cleanliness is very essential, and a mouth wash of bichloride (1 grain to 6 ounces of water) should be prescribed. The use of tobacco should be forbidden. The individual lesions should be touched occasionally with the nitrate of silver stick.

4. *Condylomata* and *moist papules* are, as a rule, best treated by cleanliness and the use of a bland dusting powder. Large growths may be cauterized with silver nitrate. Painting with the following mixture is said to remove condylomata:

| | | |
|---|---|---|
| Salicylic acid, | | |
| Tinct. cannabis indica . . . . . | āā | ʒj. |
| Flexible collodion . . . . . | | ʒj. |

Condylomata may also be excised if they present a suitable pedicle. Simple clipping with the scissors usually suffices; the hemorrhage is slight, a small dressing is all that is needed, and the wound heals well.

5. *The Eye.*—When syphilitic iritis is present, it is necessary to administer constitutional treatment in the most energetic manner possible—best, by the method of injection. In addition, the pupil should be kept dilated by the use of atropine.

**The General Management.**—The patient is generally first seen after the appearance of a suspicious genital sore; and the physician's first duty is to use every possible means, microscopic examination for Schaudinn's organism being one of them, to make a positive diagnosis. If this cannot be made, no treatment should be used; the patient should return for frequent examination so that the evolution of the sore may be followed and constitutional phenomena seen as early as possible. The moment the diagnosis is made, treatment should be instituted. One may begin with proto-iodide pills, gr. ¼ three times a day. This is, however, a *small dose*, and must be increased very soon until the patient is receiving at least 1½ to 2 grains a day. The usual error is to prescribe proto-iodide in too small rather than too large amounts. Inunctions may also be ordered, particularly if compromising lesions are present on the face. The patient should be carefully watched at first in order to determine how the mercury is being borne, and the dose should, if possible, be pushed to the point of toleration. This will require experimentation. If the method of ingestion is badly borne, injections may be tried; some patients take one form well and others another, and the method of choice must depend on the reaction of the patient. The general health of the patient must be cared for; the mouth and teeth scrupulously watched. Regular Turkish baths should be ordered; and if the patient can afford it, frequent trips to mineral baths, both for change of scene and for specific therapeutic effect, may be of value. Early in the secondary stage iodides should be ordered in addition to the mercurial treatment. Often the case will run along smoothly, but many patients will tolerate mercury poorly or will neglect their treatment; and these cases will require all the therapeutic resources which have already been mentioned.

Whether mercurial treatment should be continuous or symptomatic is a point which has been disputed. Continuous treatment is the plan advocated by Hutchinson, Keyes, and others. The drug is pushed just short of salivation in order to determine the toxic dose; and then is continued at a slightly lessened dose until active symptoms subside. It is then given in smaller amounts (the so-called tonic dose) throughout the disease, the appearance of symptoms being the indication for increase of the dose. The patient is thus kept steadily under the influence of the drug until the end of the second year.

Others advise what is known as the symptomatic or opportunist method. This is based on the theory that specific treatment acts on luetic lesions, but not on syphilis itself, and that the results of treatment limited to the periods when the disease is actually manifesting itself are satisfactory. Each successive outbreak is regarded as a recrudescence of the disease and is vigorously treated; between "relapses" specific treatment is stopped and the administration of tonics substituted. In this way, it is claimed, the establishment of a tolerance to mercury does not occur. It is, however, quite untrue that mercury acts only on the symptoms of syphilis; and the opportunist method of treatment, besides being unsound in principle, is to be heartily condemned on account of its failures and disasters in practice.

The most rational plan, as well as the one which has given the best clinical results, both as regards the cure of secondary symptoms and the prevention of tertiarism, is the one advocated by Fournier. This is known as the method of chronic intermittent treatment. Syphilis is a specific infection continuously present, symptoms or no symptoms; but the stomach will not

stand mercury indefinitely, and the body, before long, renders mercurial treatment less and less effective by establishing a tolerance to it. For these reasons prolonged treatment, combined with regular periods of rest, is the most rational plan to pursue. The syphilitic patient, when first seen, is put on vigorous mercurial treatment for about two months. If no symptoms are present a rest of about four weeks is then given, when treatment is resumed whether symptoms are present or not. The second course lasts about six weeks and is followed by a second rest of two months. Medication is then resumed for six weeks and again suspended for several months, this plan being followed for three years. In this way four mercurial courses are given during the first year, three in the second, and two or three in the third. When the iodides are begun they should also be given intermittently, each course lasting about five weeks and being followed by at least a month's rest. This program is not, of course, absolute; in most instances the courses of mercury should be longer and the rest shorter than here advised; the details must be modified for the contingencies of particular cases; but the principle of chronic, prolonged, intermittent treatment must be adhered to.

Hallopeau has suggested that the scheme be modified by giving alternate courses of mercury and iodide; it is not necessary, he says, to abstain from all treatment during the required interruptions of mercurial treatment, and during these periods of rest the evolution of the disease should be attacked by iodides. It is particularly important that the treatment during the first mercurial course be vigorous, for there is evidence that energetic mercurialization at this time exerts a powerful modifying action on the future of the disease. It should also be emphasized that the method of Fournier makes it not only possible but essential that the mercury, when given, should be administered in strong therapeutic doses.

That the treatment should be prolonged is beyond all dispute; just how long it should be continued is matter for some disagreement. Of one thing there is no doubt: the closer acquaintance with the disease becomes, the more the time limit of treatment judged necessary for its cure is extended. Ricord, for instance, thought that six months' mercurial treatment followed by three months of iodides were enough; Fournier in 1873 advised two years of mercury, but later three or four years and, in some cases, even five or six; and this extension of time for treatment represents a general trend among those well informed on the subject. It seems safe to say that mercurial treatment should be continued (intermittently) at least three years; continuance for four years is not unwise, and is perhaps the safest plan. The iodides may be continued, in courses, a year or so longer, and there seems, indeed, no good reason why regular bi-yearly courses of iodides should not be taken indefinitely.

**Serum Treatment.**—This has been discussed above. The method, although promising, offers the physician at present no help in treatment.

**Hereditary Syphilis.**—The mercurialization of the mother during pregnancy has already been dwelt upon; it remains to consider the treatment of an hereditarily syphilitic infant. The child should, in the first place, be nursed by its mother whenever possible, both to avoid infecting other women and because the mortality among artificially fed luetic infants is enormous. The treatment of the mother, which is a fairly efficient treatment of the nursing infant, should be continued throughout lactation. If symptoms appear (coryza, marasmus, eruption) the child itself must be given mercury,

which is best administered in inunctions. About 10 grains of the mercurial ointment (for an infant a few weeks old) are smeared daily on the abdomen, under the binder. It is absorbed rapidly. Gray powder may also be used in doses of ½ to 2 grains (0.003 to 0.12 gm.) thrice daily, given with sugar or milk. Mercurial baths (10 to 30 grains of corrosive sublimate to an ordinary baby's tub of water) may be employed, the child being "soaked" for ten to twenty minutes every other day. The local lesions may be treated with mild ointments; blue ointment mixed with 8 parts of vaselin is appropriate. It is particularly important to keep the child under observation during dentition and puberty.

# CHAPTER XIII.

## INFECTIOUS DISEASES OF DOUBTFUL NATURE.

By THOMAS R. BOGGS, M.D.

### FEBRICULA.

**Synonyms.**—Ephemeral fever; febris herpetica; Leichteserkältungsfieber; simple continued fever; ardent fever.

**Definition.**—Under the above and many other titles is included a group of acute fevers characterized by a brief course of from one to several days and the absence of the diagnostic features of the specific infectious group.

**Historical.**—With the steadily increasing refinement of diagnostic methods and consequent sharper definition of diseases on an etiological basis this somewhat anomalous and indefinite group has undergone a constant and gradual contraction. The older writers devoted much space to its consideration under such names as synochus simplex, febris sanguinea, febris continua simplex and the like, including in it many cases of mild atypical typhus and typhoid fevers and others which we are no longer able to recognize. And it was only in the nineteenth century, following the work of Louis and his pupils and crystallized in the classic descriptions of Murchison, that this group was reduced to something like its present proportions. When all allowance has been made, however, for errors in diagnosis and aberration from type in specific fevers, there yet remains a number of cases which must be classified under one or another of the above titles.

**Etiology.**—The causative factors are varied and indefinite. It is, in fact, our ignorance of the relation of specific microörganisms or toxins to these cases which compels us to accept such a classification as the above.

In general it may be said that the young are particularly affected, the overwhelming majority of cases falling in the first two decades. The changeable seasons of the year show the greatest number of cases, while sudden exposure to great heat or excessive cold is frequently the determining factor. Vigorous persons of full habit more often suffer than those less robust.

Individual susceptibility plays undoubtedly an important role. There are many persons whose heat-regulating mechanism seems particularly unstable and in whom slight dietary indiscretions, emotional and intellectual excitement, or bodily fatigue, may be followed by a marked rise in temperature of greater or less duration, and, so far as we can determine, entirely unassociated with any localized infection or inflammation. It is this class perhaps which furnishes the best examples of the ephemeral fever in the stricter sense, that is, of only twenty-four to thirty-six hours' duration.

Abortive types of the acute infectious disorders are often necessarily classed as febricula in the absence of the characteristic features. Such

cases are particularly frequent after epidemics of diphtheria, scarlet fever, typhoid, or measles. Here we have only the prodromata with fever of a few days' duration and rapid convalescence. In this subgroup also, in all probability, belong most of the cases of febris herpetica described by Continental writers as occurring sporadically and in epidemics and distinguished from other cases of febricula by the frequent or constant appearance of herpes labialis during the fastigium or defervescence. The proportion of these abortive specific disorders, formerly classed with ephemera, has been greatly reduced in recent years.

The Grüber-Widal agglutination test and the more general use of blood cultures for diagnosis have led to the recognition of many cases of typhoid fever in which clinically no such determination was possible. Particularly interesting in this connection are certain epidemics and sporadic cases of paratyphoid and paracolon infections. The virulence of these organisms is extremely variable and we see every gradation in the clinical picture, from the mildest simple continued fever to a classical typhoid. Very often indeed the agglutination alone is not sufficient to separate the cases clearly, but the organisms can be cultivated from the blood with comparative ease. There is little doubt that many of the mild epidemics of continued fever described in England, in the Mississippi Valley, and the South Atlantic States were due to some member of this large and complex group of organisms.

Again, the newer methods for staining the malarial parasite have led to the recognition of many cases formerly undiagnosed, in which the characteristic paroxysms were absent or so modified by imperfect quinine therapy that the typical clinical picture was lost. In another group of cases the demonstration of influenza bacilli in large numbers in the sputum or nasal secretions has made definite diagnosis possible. In still others cultures from the blood, urine, or fæces have brought to light organisms more rarely found in human pathology, such as *B. pyocyaneus, B. coli,* and members of the proteus group. It is not improbable that the rapid advance in the study of the chemical processes associated with disease will enable us eventually to distinguish accurately certain types of intoxication by the examination of the urine or the blood.

Some authorities maintain that rheumatic fever may occur without any localizing manifestations and in a mild and abortive form. Central and abortive pneumonia in children unquestionably swells the list.

Gastro-intestinal disturbances account for perhaps the major part of the simple fevers. In fact, "gastric fever" is a very common synonym in England and America. The absorption of toxins in the food, or those produced by fermentation or imperfect metabolism, is not infrequently accompanied by fever. This is especially common in childhood and, where the toxin is a recurrent factor, may give rise to a more prolonged continued fever. The stomach and intestines are normally very tolerant of partly decomposed food, and in most of these cases there must be some primary disturbance, reducing the bactericidal and digestive powers to a greater or less degree. The lumbricoid fever of French authors probably belongs in this class.

Noxious vapors and sewer gas are held accountable for febrile paroxysms in certain instances. Just how these act is unknown, but clinically some very acute cases follow quickly on exposure to such influences. Analysis of the gas from sewers and cesspools does not reveal any specially toxic substances as a rule. It may be that in some of these cases the disgust,

nausea, vomiting, and emotional disturbance set up by very putrid and stinking exhalations may definitely affect the heat-regulating mechanisms.

Tropical heat is apparently responsible in a large measure for the incidence of ephemera, simple continued fever, and ardent fever in the warm countries. Those alien to the soil and unacclimatized are particularly affected, and we have all gradations of severity from mild fever of one or two days to the most severe and fatal heat prostrations. The reluctance with which many Europeans living in the East relinquish the habit of eating and drinking, of dressing and exercising just as at home, makes them especially open to attacks of this character. In a mild degree this type of fever is quite frequent in the winter resorts of the extreme south of Florida and the Bahamas.

**Pathological Anatomy.**—The autopsy findings may reveal some definite lesion, such as central pneumonia, typhoid ulcers or general septicæmia, and so enable us to determine the true nature of the affection. In other cases nothing more than general congestion of the viscera, with more or less œdema and exudation into the serous cavities, can be found. There is no specific anatomical picture associated with this group.

**Symptoms.**—Sudden onset with chilliness or definite rigor is very common, the temperature rising quite rapidly and reaching a moderate or even high grade, 103° to 105°, in twenty-four hours. No definite incubation period is recognizable ordinarily, although in many instances it may coincide with that of some prevalent epidemic. The acute onset is especially characteristic of ephemeral fever, while simple continued fever is often preceded by a period of lassitude, loss of appetite, and slight headache, followed by a rather slower rise of temperature and a longer course. Accompanying the fever there is often some pain in the back and limbs, restlessness, insomnia, or drowsiness. The tongue is heavily furred, the urine scanty, and constipation is the rule, or less frequently a slight diarrhœa. In children the tendency to cerebral symptoms is more marked, delirium and even convulsions being not infrequent in the first twenty-four hours. The tonsils and pharynx are sometimes slightly inflamed and there may be a slight bronchial involvement. Fugitive erythema has been observed and sudamina over the chest, back, and abdomen. Labial and nasal herpes is frequent, appearing more commonly just before or during the defervescence. French and German writers separate these cases to form a group called febris herpetica, but the multiplication of terms is hardly justifiable.

The decline in ephemera is usually rapid on the second to the fourth day, and accompanied by profuse perspiration and critical discharges from the kidneys and bowels. Occasionally vomiting or epistaxis may occur at the crisis. In other cases the decline is slow and uneventful. In contrast to influenza there is commonly little if any residual depression or prostration after the crisis. In the simple continued fever the course is from six to eight or even ten to fourteen days. The temperature is not so high and shows quite marked daily excursions. It may even be remittent or intermittent. The pulse is moderately rapid, full, and strong. There is some headache and more rarely delirium. The decline is often by lysis. Many of these cases are abortive typhoid and paratyphoid infections, such as, for instance, the "Florida fever" of the Southern United States.

The "ardent fever" of the tropics is a severer form, occurring in newly arrived young persons. In it the cerebral symptoms are more marked, acute delirium being common, and may be followed by coma and death

about the tenth day in not a few instances. The majority have a well-marked crisis and recover. It is quite certain, however, as pointed out by Manson and others, that many cases of so-called ardent fever are in reality fulminant malarial infections in which the mild prodromal features have been overlooked.

**Diagnosis.**—At the onset and during the course of the disease we usually suspect something of a graver nature, and it is only after the entire course has been reviewed and all local and specific causes have been found wanting that we arrive at a diagnosis by exclusion.

**Prognosis.**—The prognosis in ephemeral and simple continued fever may be said to be uniformly good. A considerable mortality, however, is attributed in the tropics to ardent fever.

**Treatment.**—This is essentially symptomatic. Calomel and a saline may be indicated at the beginning, with cool or cold sponge baths when the temperature is high, and an ice-bag to the head in cases of headache, delirium, or epistaxis. The drinking of water should be encouraged, and acidulated mixtures may be of benefit. Salol and phenacetin are useful when there is much pain. Restricted liquid diet is best suited to all types, with rest in bed until convalescence is established.

## GLANDULAR FEVER.

**Synonyms.**—Acute cervical adenitis; Drüsenfieber; fièvre ganglionnaire.

**Definition.**—A disease of children characterized by acute onset with fever, slight congestion of the tonsils and pharynx, accompanied by swelling, tenderness, and more rarely suppuration of the cervical lymph glands, especially of those lying behind the upper portion of the sternocleidomastoid muscle. Enlargement of the liver and spleen is common and acute nephritis sometimes occurs. Constipation is frequent, although diarrhœa may mark the onset. The disease is contagious and occurs most frequently in localized epidemics. The course is mild and complications are few.

**Historical.**—The disease was first carefully described by E. Pfeiffer[1] in 1889, although cases had been noted and incompletely studied some years before. This priority is claimed for Filatow, Rauchfuss, and Korsakoff, but it is Pfeiffer's work which first drew the attention of the profession, and but little has been added to our knowledge of the disease since its publication. Other observers have contributed studies of cases and epidemics and noted the more unusual complications, such as the occurrence of suppuration and of nephritis. Neumann in 1891 observed a series of cases characterized by unilateral involvement and frequent abscess formation, and considered them as a different clinical entity. Comby also reports a large percentage of suppuration and constant unilateral infection, but classes the cases with those of Pfeiffer. Park West[2] gives valuable statistics of the largest epidemic yet studied, with a report of 96 cases. The thesis of Gourichon[3] and the exhaustive treatise of Korsakoff[4] cover the greatest part of the literature to date.

[1] *Jahr. f. Kinderheilk*, 1889, Bd. xxix, p. 257.
[2] *Arch. of Pediat.*, 1896, vol. xiii, p. 889.
[3] *Thèse de Paris*, 1895.
[4] *Arch. f. Kinderheilk.*, 1905, Bd. xli and xlii.

**Etiology and Pathology.**—Glandular fever is a disease of infancy and childhood, most of the cases occurring between the first and tenth years. Adults are rarely affected, although one or two garrison epidemics as well as isolated cases have been noted. The two sexes appear equally susceptible. Most of the cases occur in the late winter and early spring months and exposure doubtless plays some part as a determining factor. Many cases have followed other diseases, such as influenza, measles, and scarlatina, and it is probable that lowered resistance and malnutrition are contributory causes. In a large number of instances, however, there is no history of previous disease. Enlarged tonsils and adenoids have been frequently noted in association with glandular fever.

Bacteriological reports are conflicting. Neumann and Comby found streptococci in the pus from a number of suppurating cases, while others report staphylococci, influenza bacilli, and pneumococci. Cultures from the tonsils and mucous membranes have yielded equally various results. Lublinski[1] in a recent paper considered the disease as merely one type of streptococcus infection involving principally the pharyngeal tonsil.

Von Starck emphasizes the importance of the constipation and gastro-intestinal symptoms, and considers that the disease is an auto-intoxication primary in the intestinal tract. That the disease is contagious is hardly to be doubted. House epidemics are common and there may be many local foci in one community. The frequency of slight inflammation of the tonsils or pharynx, with some pain on swallowing and the characteristic involvement of the glands which directly drain this area, point to this region as the portal of entry. The severity and extent of the subsequent adenitis would seem dependent on the toxicity of the organisms and the condition of the patient. Thus in some instances we have general infection, as indicated by the involvement of many groups of lymphatics, in others only a localized process.

The occurrence of cervical adenitis, with some inflammation of the tonsils or pharynx, and occasionally severe nephritis, has suggested to some observers that the disease was abortive scarlatina or diphtheria. But so many of the cases have had one or both of the diseases either before or after the attack of glandular fever that this hypothesis has little to recommend it. The incubation period is unsettled. In many cases it seemed to be from seven to ten days. The number of fatal cases is so small that there have been no thorough studies of the structural changes in the glands. In Korsakoff's case there was acute glomerular nephritis with injection and hyperplasia of the cervical, peribronchial, and mesenteric glands, and of the splenic follicles.

**Symptoms.**—The onset may be sudden, with fever, headache, loss of appetite, and constipation, or in other cases preceded by two or three days of fretfulness and general malaise. The temperature elevation is usually moderate, 101.5° to 103°, but may reach 104°. It is commonly remittent, being highest in the evening. The pulse and respiratory rates are proportionally increased. The tongue is furred and in most instances a slight reddening or injection of the tonsils and pharynx is found. Occasionally a very slight, filmy exudate is demonstrable on one or both tonsils. Nausea and vomiting sometimes mark the initial period and constipation is present in the majority of cases. Diarrhœa may occur, however, and was considered by Pfeiffer as related to involvement of the abdominal lymph glands. Within

[1] *Zeit. f. klin. Med.*, 1907, Bd. lxii, pp. 170-178.

twenty-four to forty-eight hours after the onset, as a rule, swelling of the glands under the sternomastoid muscle is evident, although this may be delayed until the fourth or fifth day. The glands increase rapidly in size and may be as large as an olive. They are discrete, commonly firm to touch, and very sensitive. The skin over them is normal, as a rule. Torticollis and pain on swallowing frequently accompany the swelling. Bilateral involvement is the rule, but unilateral involvement is also noted. In Pfeiffer's cases the swelling appeared first on one side and then involved the other, and the course has been similar in most other reports. Comby and Neumann, however, report unilateral swelling as characteristic of their cases.

As the glandular swelling reaches its maximum the fever declines by crisis, with occasional critical discharges from the bowels (Park West), or by lysis, while the swelling persists, disappearing slowly in the course of two to four weeks. In many instances there is a recrudescence with fever and general symptoms, with the involvement of fresh groups of glands, as axillary, inguinal, mediastinal, or mesenteric. Those first involved may also increase in size with the re-invasion. Other cases are described in which there have been several recurrences of the disease at intervals of weeks or months.

Enlargement of the spleen and liver is very common, although in some epidemics this feature is absent. The respiratory system is not affected, as a rule, although in rare instances the swelling of the peribronchial and mediastinal glands may be so marked as to give modified breath sounds. Slight cough at onset is not infrequent. Pain and tenderness in the umbilical region is associated with the involvement of the mesenteric glands in some cases. Erythema, urticarial eruptions, and herpes have been noted in a few instances. Suppuration is an uncommon complication and yields readily to incision and drainage. Isolated instances of otitis media and parotitis have been recorded. Nephritis has been noted in a small percentage of the cases and is the most important complication. It appears usually in the first few days of the disease and is of a hemorrhagic type. Most of the cases end in recovery; some become chronic and a few have been fatal. In case the nephritis begins late in the disease there is a recrudescence of the cervical adenitis very like that associated with post-scarlatinal nephritis.

**Diagnosis.**—It is not until the characteristic glandular involvement has become evident that the disease may be recognized. Secondary adenitis from outspoken local causes should be rigidly excluded. Thus caries or abscesses of the teeth, thrush, follicular tonsillitis, pharyngitis, otitis media, etc., may cause swelling of the glands. But in glandular fever the involvement is out of all proportion to the local signs and it is the particular group draining the tonsil which is especially involved, while in the other infections the distribution is apt to be irregular.

The slow development, persistence, and often painless character of the tuberculous adenitis render it easy of recognition ordinarily. There is no doubt, however, that cases of glandular fever seen late after the febrile stage have been mistaken for tuberculosis. In such cases time and, where possible, tuberculin will clear up the difficulty. The torticollis and pain on moving the head, with very slight glandular swelling, easily overlooked, may lead to a diagnosis of meningitis at first.

Where a rash is present the diagnosis may be very difficult if not impossible, until the course of the disease makes it evident from the appearance of the characteristic swellings. The early development of nephritis may cause

suspicion of scarlatina in which the rash has been overlooked. The adenitis of Hodgkin's disease, mumps, or syphilis should offer no serious difficulties.

**Prognosis.**—The prognosis is almost uniformly good. A very few fatalities are recorded, due to nephritis or endocarditis.

**Treatment.**—The patient should be isolated from other children where practicable, to prevent the spread of the disease. Rest in bed is indicated, especially on account of the danger of nephritis, and should be maintained until the temperature is normal. The diet should be light and such as the patient can take readily. Antiseptic sprays and gargles may be used to advantage, with ice-bags or warm fomentations to relieve the pain in the neck. Various authors recommend antipyretics, quinine, phenacetin, etc., given by mouth or hypodermically. Calomel, recommended by most observers, is condemned by Park West as weakening the patients and causing delay in convalescence. Tonics, fresh air, and good food are indicated in convalescence. Iron may be necessary in cases with secondary anæmia.

## INFECTIOUS JAUNDICE.

**Synonyms.**—Epidemic catarrhal jaundice; Weil's disease; bilious typhoid.

**Definition.**—There are several types of acute infectious icterus characterized in general by a sudden febrile onset with pronounced gastro-intestinal symptoms and rapidly developing jaundice, sometimes accompanied by enlarged and tender liver and spleen, with albuminuria and severe nephritis. In some epidemics delirium and coma are frequently observed. The course is from a few days to three weeks, and usually terminates in recovery.

**Historical.**—Cases of acute infectious icterus of a benign form have long been recognized and epidemics more or less carefully described, notably by French observers and by Weiss in 1866. In 1886 Weil[1] published the first thorough study of the epidemic type based on four cases which came under his observation. He emphasized the acute onset, rapid and extreme development of jaundice, with tender and enlarged liver and spleen and accompanying nephritis, and pointed out the tendency to relapse. Since his publication, the German writers have reported many similar cases and epidemics and have called the disease by his name. Many English and French authorities, however, demur to the designation of Weil's disease as separate from other types of benign infectious jaundice.

**Etiology.**—The question of the specific organism can as yet hardly be considered settled. Jaeger described a bacillus of the proteus group as the pathogenic factor in a garrison epidemic at Ulm in 1892. This organism, which he has named *Bacillus proteus fluorescens*, has been found by other observers in Germany and elsewhere. It has been cultivated from the urine of the patients and from the organs of fatal cases. Jaeger and others found it also in the water supply used by the patients for bathing and drinking.

This proteus has been shown to be pathogenic for laboratory animals when injected into the veins or the peritoneal cavity, but not by feeding the cultures. Animals dead of the infection showed icterus, general parenchymatous changes and foci of necrosis in the liver. Blood cultures during life, however, have been uniformly negative for this organism. It is to be

[1] *Deut. Arch. f. klin. Med.*, 1886, Bd. xxxix, p. 209.

noted that other organisms have been reported from cases presenting the same clinical picture, especially the colon bacillus and other members of the hog-cholera group. Cases reported in the French literature have frequently been ascribed to colon-bacillus septicæmia. In view of the above facts it would seem that while Jaeger's organism may be a causative factor, it is probably not the only one.

The disease is most frequent in the second and third decades and nearly 90 per cent. of the reported cases are males. A number of single cases and small epidemics affecting children have been noted (Weiss, Wassilief, Kiesel, and others) and some even in sucklings.

The eating of rancid cheese and partially decomposed meats has been a factor in some epidemics. In fact, many of the French authorities consider the disease essentially a ptomain poisoning and not a general bacterial infection. It is certain that toxic substances like toluylenediamin in animals may produce a picture very similar to that after bacterial infection with Jaeger's organism. The incidence is greater in the spring and summer months and in wet seasons. Those exposed to foul water, as workers in ditches and sewers, soldiers, agricultural laborers, and butchers, seem most frequently affected.

**Pathological Anatomy.**—Relatively few of the cases have come to autopsy, and of these some are undoubtedly icterus gravis or acute yellow atrophy. In fact, the group here described stands between simple catarrhal jaundice and grave destructive icterus, and there are all grades of transition toward the extremes. The pathological findings in general are marked jaundice of the tissues, with wasting, slight enlargement, and cloudy swelling of the liver and spleen, sometimes with small foci of fatty degeneration in the former. The kidneys show a diffuse, tubular nephritis; no characteristic lesions of the intestine. Hemorrhages into the spleen and the serous cavities have been described. The small bile ducts are swollen and the mucosa degenerated.

**Symptoms.**—The onset is usually quite sudden and may be fulminant. Occasionally, however, prodromata, lassitude, headache, and loss of appetite precede the attack. The patient is seized with a rigor or there may be no chill. The temperature rises quickly to 103° or 104°, and the pulse is at first rapid and then slower after the appearance of the jaundice. Gastro-intestinal features are prominent at the onset, griping pains, nausea and vomiting, and diarrhœa being common. In the course the stools may be first rich in bile and then clay colored. The nervous manifestations are also marked. Headache, dizziness, pains in the back, and especially in the calf muscles, may be intense. Prostration is rapid and extreme. Delirium is very frequent. Drowsiness and even coma may rapidly follow and the picture is like the "typhoid state," developing, however, more rapidly than in typhoid fever. Jaundice begins to appear about the second to the fourth day and rapidly becomes intense. The liver is slightly enlarged and tender and the spleen usually swollen. Herpes, diffuse or macular erythema, and urticaria may be seen. A tendency to hemorrhage is frequently noted. Epistaxis, slight hæmoptysis, bleeding from the stomach or bowels, petechial eruptions and bloody exudates into the serous cavities and joints have been described. The albuminuria is usually of a considerable grade, and hyaline and epithelial casts in large number are usually present. The urine contains great quantities of bile pigments and sometimes red blood cells. Bronchitis

is conspicuously infrequent. After four to nine days of rather steady elevation the temperature begins to remit markedly and falls slowly to normal in about five to six days. The jaundice and the muscle pains disappear more slowly; the latter may be marked well into the convalescence. The liver and spleen tumors subside and the nephritis gradually clears up.

Convalescence is usually protracted and the loss of weight is often very great, from ten to twenty pounds in adults during the febrile period. In a large proportion of the cases (about 40 per cent.) there is a relapse occurring from three to eight days after the temperature first becomes normal. It is a milder repetition of the initial paroxysm and lasts five to eight days. The persistence of the splenic tumor after the first paroxysm is thought to be indicative of a relapse.

There are many abortive and mild cases which would hardly be recognized except during epidemics. Fatal cases are rare and some of those so described are not properly included in this group. Some few die from acute nephritis and uræmia, others with heart failure or intoxications of the central nervous system, and, more rarely still, after the development of pneumonia.

**Diagnosis.**—Weil's disease is a type of infectious jaundice in which fever, enlargement of the spleen and liver, nephritis, and muscular pain accompany the icterus. But there are so many similar sporadic and epidemic cases in which one or more of these features may be wanting that it seems hardly justifiable to separate this group sharply from all the others. Fr. Müller, in his comprehensive study of the "swamp fever" epidemic near Breslau, has raised the point as to jaundice being essential to the diagnosis of Weil's disease. His cases correspond in all features except the icterus.

From typhoid fever it is differentiated by its sudden onset, briefer course, and the rarity of jaundice in typhoid. In the fatal cases there are no lesions typical of typhoid fever. The Widal test is of little value, as any jaundiced serum may cause agglutination of the typhoid bacillus. It is perhaps in such cases that the deviation of the complement, as developed by Neisser and Wechsburg, might be of diagnostic value. Simple catarrhal jaundice lacks the features of general infection. The demonstration of the specific spirillum of Obermeier will differentiate relapsing fever. The resemblance to dengue and mild cases of yellow fever is rather striking, although the greater joint involvement and widespread epidemic character of the former should prevent serious confusion, while the exclusion of the specific intermediate host, *stegomyia*, and the frequent occurrence of epidemic jaundice in regions where yellow fever is unknown would reasonably exclude the latter possibility. From icterus gravis and acute yellow atrophy only the course of the disease and the absence of destruction of the liver can fully differentiate these benign cases, and there is, in fact, a gradual merging of the types and no distinct border line.

**Treatment.**—Absolute rest is necessitated by the patient's condition and should be protracted into convalescence. A diet of milk and light broths should be maintained during the febrile period. Hydrotherapy is often helpful, forced water drinking, enemata, and subcutaneous infusion of salt solution being indicated in the more toxic cases. Cool baths and ice-bags during the height of the fever are to be recommended. Warm stupes and fomentations greatly relieve the muscular pain. Strong purgatives and alcohol are contra-indicated and intestinal antiseptics are of little or no value. Small doses of calomel may be useful in special cases.

After convalescence is established the diet should be increased gradually and every effort made to build up the patient's strength and repair the tissue waste.

## MILIARY FEVER.

**Synonyms.**—Sweating sickness; suette miliare; Schweissfriesel.

**Definition.**—An acute infectious disease occurring in localized epidemics of short duration and exceedingly variant severity. The onset is abrupt, with or without prodromata, the cardinal symptoms being fever, excessive continuous sweating, great anxiety and oppression, with rapid and often tumultuous heart action and respiratory distress. On the third or fourth day an erythematous rash appears, accompanied by miliary vesicles and sudamina. With the appearance of the rash the fever subsides gradually and slow recovery follows, or death may ensue in a few hours to three or four days after onset.

**Historical.**—There is little reason to doubt the substantial identity of the miliary fever of to-day with the "sudor anglicus" or sweating sickness which swept over England in five epidemics between 1485 and 1557. These plagues differed from the present type of the malady in their wide and rapid dissemination, briefer course, greater mortality, and the absence of the rash. Most of those affected died or had a favorable crisis within the first twenty-four hours. The absence of the rash is explainable by its normal late appearance and frequent absence in the fulminant cases of the modern type. The fear of exposing the sweating body which prevailed at that period, probably accounts for the failure to observe it in the cases that recovered.

The disease spread widely over Europe in 1529 and 1551, and was then lost until the beginning of the eighteenth century, when it appeared in Northern and Eastern France as "La Suette des Picards," where it is still endemic. Hirsch has collected statistics of 194 epidemics in France between 1718 and 1874. It has also been described in Italy, Belgium, Germany, and Austria. It has never appeared in America. An important connecting link between the two types is the epidemic of 1802 in Röttingen described by Sinner. This epidemic, although localized, was in respect to lethality and clinical description identical with the English sweating sickness. Detailed historical and statistical accounts will be found in the writings of Hecker, Haeser, Hirsch, and Immermann.

**Etiology and Pathological Anatomy.**—In the absence of any known causative agent many theories have been advanced to explain the origin and localization of the disease—among others, soil and weather conditions, miasma, and malaria. In general the disease appears more frequently in the spring and summer months. It appears suddenly in localized epidemics which are of very brief duration, often not more than two weeks. In this time a very large proportion of the population may be affected.

All ages and both sexes are susceptible, although it is more prevalent among the robust. That the frequency is greater in women seems settled. The lethality in modern epidemics varies from 33 per cent. to zero and may be even so variable in different places during the same epidemic. There is some evidence in favor of the transmission of the malady by direct and even by indirect contagion, although these factors evidently play a minor role.

Cultures from the vesicles, the blood, and organs have not led to the discovery of the causative factor. Weichselbaum[1] has shown that the rapid putrefaction and subcutaneous œdema constantly noted is due to the post-mortem invasion and development of *Bacillus aërogenes capsulatus*. He has also demonstrated that the miliaria, of whatever type, are due to inflammatory processes in the skin and not to sweat retention.

There is nothing striking about the changes in the viscera. The spleen is somewhat engorged and shows cloudy swelling. The same is true, to a less degree, of the liver and kidneys. The heart is flabby and shows marked segmentation and fragmentation. There is slight swelling of Peyer's patches and often some hemorrhage in the intestine. The intestinal miliaria described by some writers are probably due to the gas bacillus. The central nervous system shows no distinctive changes beyond hyperæmia and slight increase in the cerebrospinal fluid noted in fulminant cases. Parrot and others made repeated attempts to inoculate healthy individuals with the contents of vesicles, but were unsuccessful.

In 1905 an epidemic of 126 cases occurred in Austria and is reported by Scholz.[2] He isolated a bacillus like that of Eppinger from the vesicles, but attaches little importance to it. He points out the extreme unhygienic surroundings of the patients, their houses being damp and filthy hovels without floors. Scholz seems uncertain as to the contagiousness of the disease, but suggests that it might possibly be conveyed by fleas or other vermin. All but three of his cases were women. Apparently one attack did not convey lasting immunity.

In the following year an epidemic of six thousand cases was observed by Chantemesse[3] and others in Northern France. They were too late to observe the disease at its height and, although they studied the blood and cerebrospinal fluid microscopically and made cultures and inoculations, they were without result. In their very detailed epidemiological study, however, they were led to advance the hypothesis that the disease is transmitted by fleas from field mice. They point out the great similarity in the epidemiology of miliaria and plague. The disease occurs only in country districts and usually after a rise of the streams in a wet season has driven the field mice into the villages in great numbers. Those places most affected were precisely such as had been invaded by the mice in largest numbers. At the time of the visit of the commission, however, the mice had entirely disappeared.

The invasion of villages began always with the outermost houses. Infection was much more common in those sleeping in the ground-floor rooms, especially when the rooms had only an earthen floor. Women were affected twice as often as men, possibly because their clothing gave better access to fleas.

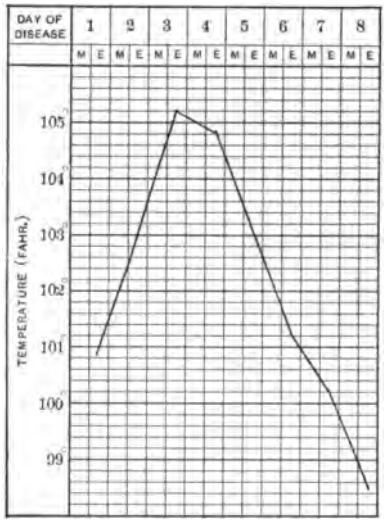
The simultaneous appearance of the disease in so many different families is only accounted for by some common source of infection with a constant incubation period. They strongly oppose the contagion hypothesis. Saizy[4] contributed a good clinical study of the same epidemic, with temperature charts and a careful analysis of the sequels of the disease.

[1] *Zeit. f. klin. Med.*, 1907, Bd. lxii, pp. 21-50.
[2] *Ibid.*, 1906, Bd. lix, pp. 542-564.
[3] *Bull. Acad. méd. de Paris*, 1906, 3d Serie, Tome lvi, pp. 293-296.
[4] *La clinique de Paris*, 1906, Tome i, pp. 435, 437, and 787-789.

**Symptoms and Course.**—The disease may be preceded by a brief prodromal stage, with malaise, headache, vertigo, muscular weakness, joint pains, and dryness of the mouth, sometimes nausea and vomiting. These symptoms usually precede the attack by a few hours only, although occasionally of one or two days' duration. Often they are altogether absent. The onset is sudden and in a great proportion of cases occurs in the night. The first symptom is sweating, although this may be preceded by a slight chill. At the same time the temperature rises and the patient feels a burning heat in the skin despite the extreme sweating.

The temperature varies with the severity of the epidemics and the individual cases. Averaging 102° to 103°, it frequently reaches 105° to 106° in severe cases, and may be even higher. The frequency of the pulse is increased out of proportion to the temperature and is further peculiar in its variability coincident with the cardiac paroxysms which are characteristic of the disease. The heart beat during these paroxysms is irregular and almost delirious. The palpitations cause the patient great anxiety. Marked pulsation and a peculiar sensation of constriction in the epigastrium are among the classical symptoms. This is generally constant to a greater or less degree and increased in paroxysms of variable intensity. Associated with it there may be tenderness on pressure. A feeling of laryngeal occlusion and impending suffocation is also very common. These phenomena are subjective and of nervous origin. The most careful examination of the heart and lungs discloses no abnormality.

FIG. 22




Miliary fever. Temperature curve. (Saisy.)

Other nervous features associated with the primary or sweating stage, although of less importance, are great prostration, delirium, clonic convulsions, and cramps in the hands and legs. The lips and tongue are dry, the breath foul, and there is marked anorexia with great thirst. Often nausea is present and less commonly vomiting. The urine is greatly reduced in volume and may be only 300 to 400 cc. in twenty-four hours. Temporary anuria is often observed. The low output persists until the sweats cease, when there is often a sudden critical discharge of urine rich in salts. Albuminuria is not common. As a rule the examination of the heart and lungs is negative, although the latter may show scattered, coarse rales. There is no leukocytosis.

Epistaxis and hemorrhages from the bowel occur frequently in some epidemics, although the bleeding is rarely serious. The rash may also take a purpuric character in such cases. There is commonly moderate enlargement of the spleen with little or no increase in the size of the liver.

The sweating is the most striking and persistent feature of the disease. It

is extraordinarily great in amount, necessitating very frequent change of linen and bed-clothes. It differs from the sweating of most febrile diseases in appearing with the onset of fever, continuing during the fever, and increasing with increase of temperature. It is probably due to toxic excitation of the medullary centres.

The eruption appears on the third or fourth day and is seen first on the neck and back, under the breasts and axillæ, and between the thighs. A general erythema is present, in addition to which appear (*a*) sudamina (miliaria alba or crystallina), (*b*) red papules becoming vesicular (miliaria rubra), (*c*) petechiæ of variable size (purpura miliaria). The appearance of the eruption is preceded by itching. The red papulovesicular type is most frequently observed, with usually some sudamina; the purpuric type is not seen so often and occurs in the cases with other hemorrhagic manifestations. Vesicles are also frequently found on the mucous membranes of the conjunctiva, nose, and mouth. The rash may come out rapidly and cover the whole body in twenty-four hours or slowly and in successive crops. Thus desquamation may be advanced in the regions first affected, while other areas show the early stages of development.

The eruption stage marks a crisis in the disease and the symptoms above noted usually abate gradually after its appearance. The fever drops with a rapidity proportionate to the development of the rash. The nervous and digestive disturbances become less and less marked and the sweating more slowly lessens, disappearing only with convalescence. Desquamation begins in two or three days after the rash appears and follows in the same order. The horny layer of the skin is thrown off as fine scales or in coarse sheets. Sometimes casts of the whole hand are seen.

Convalescence is very slow in mild as well as in severe cases. There is usually great weakness and anæmia and loss of weight. Tremor, cardiac arrhythmia, insomnia, and general nervousness are apt to persist for some time and months may elapse before the patient is fully restored.

While the course of the disease is usually favorable, it is not always so. In the fulminant cases death may ensue within forty-eight hours from the onset. In such cases extreme hyperpyrexia, dyspnœa, and very rapid pulse, with præcordial pain and constriction, are characteristic. Delirium and death from suffocation end the attack often before the rash has appeared. In other cases which begin mildly a similar development may take place suddenly on the third or fourth day before the appearance of the rash. More rarely sudden collapse occurs, with cyanosis and death in a few minutes.

In the second stage there is occasionally death following multiple hemorrhages from the nose and intestinal tract. Recrudescence is sometimes observed during the second stage, accompanied by intensification of the fever, sweating, and nervous symptoms. Relapses are extremely common in the first two weeks, and are usually milder than the primary attack.

**Diagnosis.**—This is not difficult with typical cases. The abrupt onset, sweating with fever, nervous phenomena, and the vesicular rash are peculiar to this malady. Very mild and atypical cases are sometimes confused with measles.

**Prophylaxis and Treatment.**—As the evidence points to the contagious character of the disease, patients should be isolated in order to restrict its spread. Rigid disinfection of house and clothing should be enforced. The therapy is symptomatic. The sudorific treatment still advocated by the

laity is injurious and strongly contra-indicated. The patient should be lightly covered and the room thoroughly ventilated. The wet clothes should be frequently changed.

Cold packs give much relief during the hyperpyrexia and diminish the nervous symptoms. The diet should be bland and mostly liquid, with large amounts of water. In serious cases the symptoms must be met as they arise. Atropine in guarded doses may be helpful in cases of excessive sweating and anuria. Grave nervous phenomena and cardiac delirium are best met with the careful administration of morphine. The efficacy of quinine is very doubtful and it was not used by the French Commissions in 1887 and 1906. Careful dieting and the exhibition of iron and tonics will do much to ensure complete restoration during convalescence.

## ROCKY MOUNTAIN SPOTTED FEVER.

**Synonyms.**—Tick fever of the Rocky Mountains; piroplasmosis hominis; black fever; blue disease.

**Definition.**—An acute infectious disease of man characterized by sudden onset, with chill, continued fever, headache, severe pains in joints and bones, and a macular eruption, becoming petechial, which appears first on the ankles and wrists, later spreading all over the body.

The disease is endemic in the Bitter Root Valley of Montana, appearing in the spring months, and occurs also in the neighboring mountainous parts of Idaho, Wyoming, and Nevada. It affects all ages and both sexes, and is, in the light of the evidence so far collected, not contagious. The mortality varies with location and from year to year, averaging 70 per cent. in Montana, but very much less (1 to 3 per cent.) in Idaho. It can be conveyed by the bite of the "wood tick," *Dermacentor occidentalis*, and is transmissible experimentally to monkeys, guinea-pigs, and rabbits.

**Historical.**—The disease known as "spotted fever" has been observed in the Bitter Root Valley for more than thirty years, or since the early days of permanent occupation by white settlers, the first recorded cases occurring at Woodside, Montana, in 1873. Inquiries by various authors have failed to establish any history of its appearance among the Indians, the hunters and trappers, or missionaries who first inhabited the region. In the past twenty years it has been recognized by the local physicians as a clinical entity and readily distinguished from typhus, typhoid, and other fevers. In 1896, Wood[1] published an account of the disease as communicated by various observers to him. Later, Maxey[2] and others published excellent clinical studies, but made no contribution to the pathology or etiology.

**Etiology and Pathology.**—The incidence of spotted fever is striking as to its localization and time of appearance. It occurs only in the high valleys of the circumscribed mountain regions above noted and in the spring and summer months, the cases appearing as early as March and as late as July, but the greater number falling in the months of May and June. All ages and both sexes are susceptible, but the incidence is greater in males between the ages of twenty and forty years and among those whose occupation leads them

[1] *Rept. Surg. Gen. Army*, 1896, pp. 60-65.
[2] *Medical Sentinel*, 1899, vol. vii, pp. 433-438.

afield and into the forests; cattlemen, farmers, lumbermen, and miners are most apt to be affected. The cases appear singly in widely separated places and there is little or no evidence to point to family or house infection.

The first pathological study of the disease was made by Wilson and Chowning[1] in their report to the Montana State Board of Health. In this and subsequent[2] communications it was shown that the pathological and bacteriological findings clearly differentiated the disease from any of those disorders of which it might have been considered an aberrant form such as typhus, typhoid, and cerebrospinal meningitis. Wilson and Chowning described bodies in the fresh and stained blood which they held to be hæmatozoa and named *Pyroplasma* (*Piroplasma*) *hominis*. The findings were in part confirmed by Anderson[3] (1903) and others. Subsequent investigation, however, by Stiles, King, Ashburn, Ricketts, and others has failed to substantiate the findings. Nor have Wilson and Chowning been able to demonstrate their organisms in a convincing manner. Some of the bodies they describe certainly resemble platelets, others the navicular body of Arnold, and endoglobular degenerations of various forms. In fact, to those who saw the specimens demonstrated, the wide variation in morphology and staining characteristics of the objects was very striking and far from convincing.

Similar bodies were described by these authors in the blood of the burrowing squirrel or "gopher" (*Citellus columbianus*), and they first suggested the role of the tick in conveying the disease. They also described the transmission of the piroplasma to rabbits experimentally by injecting blood from patients.

Stiles[4] (1905) published a zoölogical study of the disease and a complete bibliography. He was unable to find any piroplasma in the blood of typical cases during life or postmortem. He also failed to find them as described by Chowning and Wilson in the blood of the gopher and strongly opposed the spermophile and tick transmission theory advanced by these writers. He also pointed out the rather marked clinical variation of this disease from known types of piroplasmosis. In general the piroplasma theory has met with lack of confirmation and skepticism.

In 1906, Ricketts,[5] after exhaustive and fruitless search for piroplasma and equally careful although negative bacteriological investigations, began experimental inoculations in animals. He succeeded in transmitting the disease to guinea-pigs and monkeys by intraperitoneal injection of the blood of patients suffering from spotted fever, and finally established a constant transmission in laboratory animals.

King[6] and Ricketts[7] separately demonstrated beyond doubt that the ticks, *Dermacentor occidentalis*, male and female, are capable of transmitting the infection by their bites. Whether they are necessary intermediate hosts or play a purely mechanical role is not yet determined. These ticks appear with

[1] *Journal of the American Medical Association*, 1902, vol. xxxix, pp. 131–138.
[2] *Journal of Infectious Diseases*, 1904, vol. i, pp. 31–57.
[3] *Bulletin No.* 14, *Hygienic Laboratory of United States Public Health and Marine Hospital Service.*
[4] *Bulletin No.* 20, *Hygienic Laboratory of United States Public Health and Marine Hospital Service.*
[5] *Journal of the American Medical Association*, 1906, vol. xlvii, pp. 33–36.
[6] *Public Health Reports*, July 27, 1906.
[7] *Journal of the American Medical Association*, 1906, vol. xlvii, pp. 358 and 1067–1069.

the first warm days of spring and begin to disappear in June. There are none to be found in the fall. Their life cycle has been described by Ricketts under laboratory conditions, but observations on their natural development and hibernation are incomplete.

Experimental animals, surviving one attack of the disease, show a high degree of immunity to further inoculation. According to Ricketts'[1] further observations the virus is destroyed at a temperature of 50° C. in half an hour. Desiccation rapidly deprives the blood of its infectious power, but the virus can apparently withstand low temperature for a number of days. The infectious agent does not pass through Berkefeld filters. Experiments with washed red blood corpuscles, serum, leukocytes, and tissue emulsions have led Ricketts to consider that the infection is a general plasmic type and not confined to the red cells or leukocytes. Infectious blood ground in a ball-mill loses its power to produce the disease to a great extent and at the same time there is evidence of the liberation of toxic substances which pass through the filter.

The pathological findings reported by Wilson and Chowning, Anderson, Ricketts, and subsequent writers include as the main features extensive petechial involvement of the skin confluent over dependent areas, and most abundant on the arms, legs, and back. The capillaries of the skin are engorged and there is some extravasation of blood in the rete mucosum. Evidence of recent tick bites is reported in a number of cases. The cerebral and spinal meninges were normal or showed slight hypostatic congestion. No meningitis was found in any case. The lungs were normal or with hypostatic congestion; the heart flabby and friable, with small petechiæ under the epicardium. The stomach and intestines were normal. No involvement of Peyer's patches or of the mesenteric and retroperitoneal glands was found. The spleen is greatly enlarged, dark in color, and diffluent, the Malpighian bodies are obliterated, and there are many phagocytic leukocytes with red blood cells, but no free pigment. The liver is enlarged and shows extensive fatty infiltration; the pancreas is also increased in size. In every case the kidneys were large and red with small hemorrhages under the capsule and in the pelvis. The cortex was swollen and congested, but not adherent; the pyramids red and sharply defined; general cloudy swelling was evident microscopically. No lesions are noted in the bladder or genital organs. Cultures from the heart's blood and organs were sterile or showed contamination from the common agonal and postmortem invasion.

The experimental lesions in guinea-pigs and monkeys correspond in general to the above findings, although the skin involvement is much less marked, guinea-pigs showing extensive purpura of the genitalia and monkeys in some instances a petechial eruption quite like that in man.

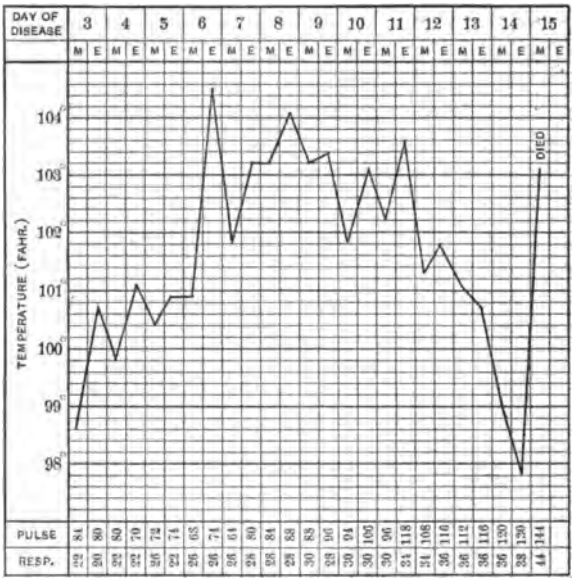
**Symptoms and Course.**—The incubation period is from three to ten days and during this time there is increasing malaise, with pain in the bones and muscles. There is ordinarily a severe chill at onset which may recur. Nausea and headache are common. The bowels are constipated and crushing pains in the limbs are quite characteristic. The tongue is furred and there is a yellowish tinge to the conjunctivæ, with deepening jaundice during the course. Nose-bleed is not infrequent at onset and may be severe in the

[1] *Journal of Infectious Diseases*, 1907, vol. iv, pp. 141–153.

second week. The temperature rises rapidly after the chill and is continuous, with but slight daily variations. It usually reaches 103° to 104° on the second day and may continue to rise in the following week and, in fatal cases, be as high as 105° to 107°. In the milder cases the temperature declines slowly after the tenth to the twelfth day and reaches normal at the beginning or end of the third week.

The pulse is characteristically very rapid, ranging from 110 to 140 in average cases and much higher in very severe ones. At first full and strong it becomes thready as the disease progresses. The respiratory rate is also increased, averaging 36 or more per minute, and rather shallow. Slight bronchitis is common and pneumonia is a well-recognized complication.

FIG. 23




Rocky mountain spotted fever. Temperature curve. (Wilson and Chowning.)

The blood shows a steady diminution of red cells and hæmoglobin during the fastigium and defervescence with regeneration after the temperature falls. The leukocytes are normal or moderately increased in number, ranging from 8000 to 14,000, with an increased percentage of large mononuclear cells. The blood is dark in color and coagulation often greatly delayed. The Grüber-Widal test has been negative in all cases.

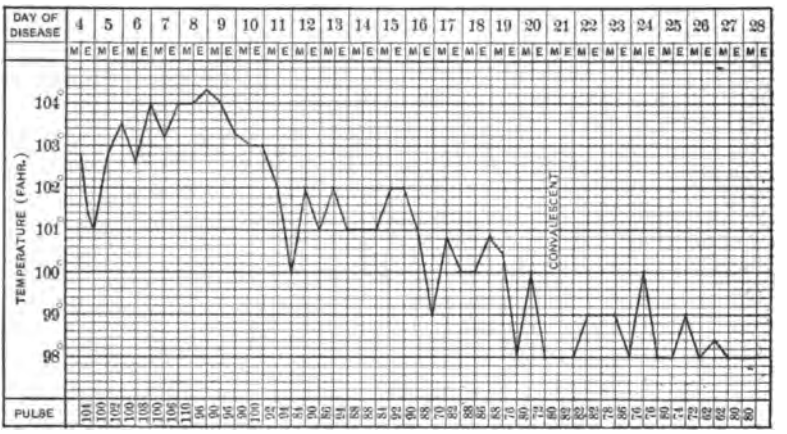
The digestive system may show little or no disturbance during the early part of the disease, but nausea and vomiting are apt to appear in the second week and may be persistent and excessive in fatal cases. Slight tympanites is not infrequent and distention may be marked shortly before death. Enlargement and tenderness of the spleen are marked and appear early. The liver is also palpable just below the costal border. There is no general

abdominal tenderness, as a rule. Hemorrhages from the nose, mouth, stomach, and bowels are not uncommon. Bloody effusions into the joints are also reported. The urine is scanty and high colored, with a trace of albumin and hyaline, epithelial, granular, and blood casts, but hæmoglobinuria is absent.

Restlessness, irritability, pain, and hyperæsthesia with photophobia are common nervous symptoms. In severe cases stupor with low delirium is frequent and coma usually precedes death. Slight opisthotonos is reported for a few cases, but muscular rigidity and Kernig's sign are absent. Convulsions have been noted rarely in children.

The rash appears on the second to the seventh day after onset, most commonly on the third day. It is first seen on the wrists and ankles, spreading toward the trunk, and is found on the forehead and breast, but especially thick over the back. The abdomen shows fewer spots and is involved later.

FIG. 24


DAY OF DISEASE
4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28
M E M E M E M E M E M E M E M E M E M E M E M E M E M E M E M E M E M E M E M E M E M E M E M E M E M E M E M E
TEMPERATURE (FAHR.)
104°
103°
102°
101°
100°
99°
98°
CONVALESCENT
PULSE

**Rocky mountain spotted fever. Temperature curve. (Wilson and Chowning.)**

In the severe cases the palmar surfaces of the hands and feet and also the scalp may be thickly covered with the eruption. At their first appearance the spots are bright red, disappear on pressure, and vary from 1 to 6 mm. in diameter. These macules become steadily darker and definitely petechial. By the seventh to the tenth day they have usually reached the fullest development when the fever is also at its height. At the same time the general icterus is marked and the spots may be confluent over dependent parts, giving the skin a mottled appearance.

With the decline of the fever the spots fade, leaving a stain in the skin. Exacerbations or sweating may cause them to reappear and during convalescence a warm bath or exercise will bring them out. Often in severe cases there is gangrene of the skin over the toes, fingers, elbows, ears, and frequently scrotum and penis. Œdema is also noted over head, face, and dependent parts. Desquamation begins when convalescence is well advanced and is general, although most marked, on hands, feet, and face. Convalescence

usually begins about the fourth week and is generally slow. In a very few cases relapses have been noted. The principal complications are gangrene, above noted, and lobar pneumonia. Immunity is conferred by one attack.

**Diagnosis.**—To those who have seen the disease its recognition is easy. Its endemic and seasonal occurrence, the character of the rash and associated pain and nervous phenomena are sharply defined. From typhus fever it is distinguished by its occurrence in isolated cases in scattered communities and its non-contagious character. The onset in typhus is abrupt and the decline by crisis. In typhoid fever the occurrence in relation to water supply, the lower fever, slow pulse, diarrhœa, Widal test, and positive blood cultures make the distinction easy. In cerebrospinal meningitis, the greater prevalence in children, frequent absence of rash, more intense nervous symptoms, and the demonstration of the organism by lumbar puncture render the differentiation fairly easy. A mild type of the disease without any rash is said to exist. Its diagnosis is, however, not at all clear.

**Prognosis.**—While delirium and marked nervous features are considered unfavorable, little can be premised from the severity of the eruption or the height of the fever. In Idaho and Wyoming the mortality is very much lower than in Montana. Death occurs most frequently between the sixth and twelfth days and patients surviving the second week are likely to recover. The mortality is greater among the old and less in children.

**Treatment.**—There is no specific remedy and the therapy is symptomatic. Good surroundings with careful nursing are important. The patient should be protected from noise and have the room darkened. The diet should be liquid or soft in character until the decline of the fever. Sponge baths of cool or tepid water are helpful in reducing the nervous phenomena and lowering temperature. Phenacetin and other antipyretics are in common use. Free purgation with calomel and saline cathartics, supplemented by enemata when necessary, is recommended by most observers. Morphine may be necessary for the relief of excessive pain. The forcing of water and use of acid diuretics is indicated and subcutaneous saline infusions may be necessary in severe cases. The efficacy of quinine is not settled, the opinions being widely divergent on this point.

## PSITTACOSIS.

**Definition.**—An epidemic disease of parrots distinguished by general debility, loss of appetite, and chronic enteritis, with a high mortality. The same name is also applied to a disease in man characterized by onset like typhoid fever, with signs of severe atypical pneumonia. This malady has occurred in house epidemics and has been ascribed to contagion from sick parrots.

**Historical.**—Ritter[1] in 1879 made the suggestion that a house epidemic of pneumonia observed by him might have been due to infectious material introduced with the cage of freshly imported parrots. Similar epidemics were described by Ost (1882) and by Wagner (1882–86), but it was after the first Paris epidemics of 1892 and 1893 that the disease attracted general interest.

[1] *Deutsch. Arch. f. klin. Med.*, 1879, Bd. xxv, p. 23.

In the epidemic of 1892 there were 49 cases with 16 deaths. The incidence of the infection was strikingly associated with the importation and subsequent disposition of a number of South American parrots. A large number of the parrots died of enteritis on the voyage and of the remainder many were sick. They were distributed in two lots which formed the foci for the epidemic. The first case appeared twenty-six days after the arrival of the birds and was succeeded rapidly by others, in each instance occurring in houses where one or more of the infected parrots had been sent. The cases developed often simultaneously in several members of the household soon after the arrival of the birds.

During this epidemic Peter first characterized the disease as "typhus des perruches." Smaller epidemics followed in 1893, 1894, and 1895–96. In Italy similar house epidemics, associated with the importation of parrots, were reported in 1894–95 by Banti, Palamidessi, and others. Leichtenstern reported an epidemic of 10 cases with 4 deaths in Cologne in 1898. Vickery[1] in 1904 described 3 cases, quite similar to the European epidemics, which occurred in New Hampshire.

**Etiology and Pathology.**—In the Paris epidemic of 1893, Nocard isolated a bacillus from the dried wings of parrots dead of psittacosis and showed that it was very pathogenic for parrots, pigeons, fowls, and laboratory animals. He also showed that healthy parrots could be infected by putting dried wings of the dead birds in their cages. The bacillus of Nocard belongs to the hog-cholera group, and is very similar in its cultural characteristics to the typhoid bacillus. The only case in which it was found in man is that reported by Gilbert and Fournier,[2] who isolated it from the heart's blood at autopsy during the epidemic of 1896. Other observers have failed to find the organism in man, but some have succeeded in isolating it from the bodies of parrots.

Widal and Sicard described agglutination tests for the differentiation of the organism from the typhoid bacillus. The differences are slight, however. Serum of typhoid patients agglutinated both organisms, but the typhoid bacillus was clumped in higher dilutions. Nicolle and Giraud have reported cases in which the diagnosis was based on this quantitative difference of agglutinating power.

The pathological findings in the parrots show marked enteritis with cloudy swelling of liver, spleen, and kidneys, but no pulmonary involvement. In men the principal feature of the fatal cases has been the presence of pneumonia with signs of general infection, but no specific typhoid lesions. The French reports do not include details of autopsies. Cultures from the lungs, heart's blood, and abdominal viscera have yielded the pneumococcus, streptococcus, colon bacillus, and other organisms. Nocard advanced the theory that the bacillus of psittacosis prepared the way for secondary pneumococcus infection, and this view is generally held by the French observers.

The possibility that this disease may be transmitted from parrots to man cannot be denied when the incidence in relation to the sick parrots and the simultaneous infection of whole families are taken into consideration. The bacteriological findings are, however, very contradictory and unconvincing. It must be remembered also that exactly similar house epidemics of atypical

[1] *Medical News*, New York, 1904, vol. lxxxv, p. 780.
[2] *Compt.-rend de biol.*, 1896, p. 1098; also *La presse méd.*, 1897, p. 25.

pneumonia have been recorded entirely unrelated to the disease in parrots (Leichtenstern).

**Symptoms and Course.**—The malady resembles typhoid fever complicated with pneumonia. The incubation period is uncertain, varying from seven to twenty-five days in different reports. Dubief gives the average as seven to ten days. The onset is variable: in some cases sudden, with chill, as in pneumonia; in others gradual, with prodromata of typhoid fever, headache, malaise, photophobia, loss of appetite, nausea, constipation, great lassitude, and weakness. In those who practice mouth-to-mouth feeding of parrots the initial involvement may be a diphtheroid stomatitis, with enlargement of the submaxillary glands.

The rise of temperature is usually rather rapid, reaching 102° to 104°. The fever is continuous with daily remissions. The pulse varies from 100 to 120. From the first there is cough, muco-purulent sputum, and increased respiratory rate. On auscultation, fine moist rales are heard throughout both lungs. There is usually no evidence of consolidation at the time of onset. The tongue is dry and furred and the breath foul. Abdominal symptoms are not marked. The spleen is, however, enlarged and, rarely, scattered rose spots or petechiæ are seen. Diarrhœa or constipation may be present, the former being more common. Nausea and vomiting are not usual except at onset. The patient is dull and stupid, with more or less marked delirium.

In uncomplicated cases the duration of the disease is fifteen to twenty days and the prognosis is generally favorable. With the development of pneumonic symptoms the aspect is graver and to this factor the high mortality is due. The pneumonia may be frankly lobar or lobular and may involve different areas in succession. The sputum becomes rusty or bloody and the cough incessant, with marked pain in the chest.

**Diagnosis.**—The recognition of the disease is difficult, and it depends principally on the association of house epidemics with the presence of diseased parrots. The clinical picture is not sharply differentiated from atypical pneumonia. Specific agglutination and blood culture would separate cases of typhoid fever. Severe influenza has many points of similarity and the first Paris cases were so diagnosed by Dujardin-Beaumetz.

**Prognosis.**—The average mortality is between 35 and 40 per cent., being highest in old people and notably less in children.

**Treatment.**—In view of the possible agency of the parrot in conveying this infection the handling of sick birds should be discouraged. Cleanliness and disinfection of the cages should be carefully observed. The patients should be isolated as a precautionary measure. Tub baths and cold packs are highly recommended by the French observers, who treat the cases throughout like typhoid fever.

## FOOT AND MOUTH DISEASE.

**Synonyms.**—Aphthæ epizoöticæ; aphthous fever; Maul und Klauenseuche; fièvre aptheuse.

**Definition.**—An infectious disease of cattle and other domestic animals, the characteristic features of which are moderate fever, disappearing with the development of a vesicular eruption on the mucous membranes of the

mouth and on the skin above the hoofs and between the toes. Ulceration follows, with salivation and great tenderness of the affected parts. Loss of appetite and great emaciation accompany this stage. Healing is slow, but most animals recover. Fatal apoplexy is not uncommon and death from septic infection of the sores is also well known.

The malady is transmissible to man through unboiled milk or butter and cheese, and also directly from the saliva or contents of the vesicles of infected animals gaining entrance through abrasions of the skin. It is especially frequent in children and in those whose work brings them in contact with diseased cattle.

**Historical.**—The aphthous epizoötic has been recorded in Europe since the sixteenth century, although it probably prevailed much earlier, especially in the eastern part. It was first described in human beings by writers in the eighteenth century. Sagar (1765) suggested its relation to the disease in cattle and the infectiousness of the milk. During three hundred years epizoötics have been frequent and entailed great losses throughout Italy, Germany, and France. It first appeared in England about 1839 and prevailed there in frequent outbreaks until rigid exclusion of cattle from the continent was enforced and the disease was stamped out. There has been no epizoötic in England since 1892. In America the disease has never been widely prevalent. Three local outbreaks have been recorded in New England and the Middle States in 1870, 1884, and the last in 1903.[1] The infection in each instance was traced to imported cattle.

Human infection has constantly accompanied the epizoötics and its incidence is probably much greater than the reports indicate, as the milder cases were not seen by physicians. Inoculation with a mild virus has been irregularly practised for many years to prevent serious epizoötics. Its results have not been very encouraging, however.

**Etiology and Pathological Anatomy.**—The specific organism of foot and mouth disease is still unknown despite the great amount of work devoted to its discovery. Bacilli, cocci, streptothrices and protozoa have been described by different observers as the causative factor. In 1898, Loeffler and Frösch[2] demonstrated that the virus was ultramicroscopic and passed through the finest Berkefeld filters. The filtered lymph, free from all demonstrable bacteria, was capable of producing the typical lesions in all the animals susceptible to natural infection and transmissible indefinitely from them to others. This observation is amply confirmed by other observers. This discovery discredits absolutely all the previous findings of organisms of whatever sort.

The infection is spread readily by contact with sick animals or by the dung or litter or the use of stalls or drinking troughs previously used by them. It is also communicable from one species of animal to another; cattle, horses, sheep, goats, swine, deer, and even dogs and fowls are susceptible. The virus is killed by a temperature of 60° C. in a few minutes and is rapidly destroyed by drying. If kept cool and moist its virulence is unimparied for months.

The portals of entry for natural infection are not clearly established, but animals may be infected by injection of lymph from the vesicles into the

[1] L. Frothingham, *Boston Medical and Surgical Journal*, 1903, vol. cxlviii, pp. 9–12.
[2] *Centralbl. f. Bakt. u. Parasit.*, 1898, Bd. xxiii, abt. i, pp. 371–391 u. ff.

blood, peritoneal cavity, muscles, and digestive tract, or by rubbing on the scarified mucosa of the mouth. Cutaneous and subcutaneous infection is irregular and uncertain. Two to three weeks after the beginning of the attack most animals show a greater or less degree of natural immunity, which is, however, of uncertain duration. An antibody capable of protecting against a certain amount of virus is present in the serum during this time. This immunity can be greatly increased in heifers and young swine by repeated injection of virus in increasing doses, and a protective serum conveying a brief passive immunity to other animals has been made (Loeffler and Uhlenhuth). Active immunization has not been successfully carried out. The large amounts of protective serum required have made the process too expensive for economic use in cattle. Sheep and swine can, however, be protected with small doses.

Of the typical morbid anatomy of the disease, apart from complications, little is known, as few animals die from this cause directly. The vesicles form in the rete mucosum and the subsequent ulceration is usually completely healed without scar by extensions of the epithelium over it. Animals dying during the disease have shown vesicles in the œsophagus, trachea, and bronchi. Very severe grades of gastro-enteritis have also been noted with hemorrhagic infiltration and cloudy swelling of the viscera. Acute œdema of the lungs has been found in some instances and myocarditis and dilatation are described by many observers. Sudden death from apoplexy with multiple embolism is a frequent accident in very severe epidemics. In the apoplectiform type laryngeal paralysis leading to aspiration of food into the lungs is common. Nissl changes in the central nervous system have been reported. It is probable that some of these severe pathological changes are due to secondary infections. The ulcers on the feet are especially liable to secondary infection, which may lead to severe inflammation of the matrix and separation of the hoof, arthritis, bone necrosis, and general pyæmia.

**Symptoms and Course.**—In man the disease sets in with fever after variable incubation period of two to ten days. The fever is usually not very high, but may reach 104° and be accompanied by a shaking chill. Loss of appetite, languor, pains in the muscles, back, and head, with cramp-like pains in the abdomen, nausea, and vomiting are common at onset.

The primary seat of infection in man is most frequently the mouth, due to drinking infected milk. The mouth feels hot and dry and there are areas of hyperæmia over the lips, base of the gums, margin of tongue, and mucosa of the cheeks. The vesicles form about two to three days after the initial symptoms and are at first small and discrete, but tend to enlarge rapidly and become confluent. They may extend over the whole buccal mucosa and into the pharynx, larynx, œsophagus, and trachea. On the skin the blebs are often found about the mouth and nose. The conjunctiva and cornea may be involved and the skin between the toes and fingers is frequently affected. Among those working with sick cattle the borders of the nails are often attacked and severe panaritium may follow with secondary pyogenic infection. In severe cases the vesicles may be distributed over the whole body, especially about the breasts, thighs, gluteal folds, and genitalia.

With the development of the vesicles the temperature falls. At the same time the tongue and lips swell and there is difficulty and pain in swallowing and marked salivation. There may be also a profuse nasal discharge. The

content of the vesicles is at first clear, but soon becomes purulent and invaded by the mouth bacteria. The vesicles are easily broken and leave weeping, shallow ulcers, which are very painful when touched. This painful ulceration of the mouth and gullet often leads to serious inanition through the refusal of food. Speech may also be difficult. The submaxillary and sublingual lymphatics and occasionally the salivary glands may be swollen and painful. Accompanying the vesicular stage there is often colic and diarrhœa or even bloody stools in children.

The course of the disease when uncomplicated is generally mild and favorable. The ulcers become crusted over and gradually covered with new epithelium, leaving no scars except where there has been pyogenic invasion of the corium and subcutaneous tissue. The average duration is two weeks from the onset, although very mild cases may be well in less time and more severe ones last six to eight weeks. In young children the danger is greater from the severe disturbances of nutrition rendering them especially liable to severe gastro-enteritis and even death from inanition.

**Symptoms in Cattle.**—The disease, as the name indicates, may affect the mouth or feet or both. The incubation period is from two to eight days and the onset is accompanied by mild fever, loss of appetite, rough coat, and profuse salivation. In fact, veterinarians can make the diagnosis from the constant slobbering and the "smacking" noises the animals make. The mucosa of the mouth is reddened and vesicles appear about the third to the fifth day. They may reach the size of a dollar. Often they extend over the outer part of the lips and into the nose. Simultaneously there is swelling about the hoof, with subsequent formation of vesicles and ulcers. These make the animals walk stiffly and there may be severe secondary infection of the feet, with loss of the hoof or death from pyæmia. Milch cows show great loss in milk and may have vesicles on the udder or occasionally severe mastitis. In all cattle there is great loss in weight owing to difficulty in feeding and swallowing. Apoplexy and pneumonia are among the serious complications. The mortality is high with young animals, varying, however, with different epizoötics. Sheep, goats, horses, and swine are more apt to be affected in the feet alone.

**Diagnosis.**—In any case of aphthous disease the history should be carefully noted with special reference to the presence of foot and mouth disease in the neighborhood or at the source of milk and butter supply. These facts with the characteristic onset and the superficial rapidly developing vesicles would make the diagnosis certain. The common aphthæ in children are small, round, yellowish, discrete, and unaccompanied by acute general symptoms. Stomatitis ulcerosa is distinguished by the extensive and deep infiltration and rapid necrosis, especially of the gums. Inoculation of the contents of the vesicles into the mouths of sheep or swine would make the diagnosis definite in doubtful cases. The hands may be the primary seat of the vesicles in those who work with cattle.

**Treatment.**—Prophylaxis is of primary importance. Isolation and slaughter of infected herds and condemnation of the dairy products, with thorough disinfection of the stalls and troughs, should be enforced. The milk is rendered innocuous by heating to boiling. But milk from sick cattle should not be used, even if it be sterilized. The effect of serum therapy has already been noted. More recently the injection of bichloride of mercury has been recommended by Baccelli for the treatment of cattle

and widely used in Italy. The German commission has reported adversely upon the Baccelli treatment, and think it may be very harmful. It is not applicable to man.

In man it is well to isolate the patient and apply local remedies to the ulcers. Chlorate and permanganate of potassium are recommended as mouth washes and the ulcers may be touched with silver nitrate or copper sulphate. Drying powders may be applied to the external lesions. Special attention is given to the diet, and in severe cases or in young children, feeding by nasal or stomach tube or nutritive enemata may be indicated.

## MILK SICKNESS.

**Synonyms.**—Trembles; slows; puking fever.

**Definition.**—A disease primarily of herbivorous animals and transmissible to man or other animals feeding upon the milk or flesh of infected individuals. The disease is characterized by gradual loss of appetite, obstinate constipation, drowsiness, muscular tremor, and convulsions. Or it may be latent and develop fulminantly in such cases by forcing the animal to vigorous muscular exertion.

**Historical.**—This remarkable disease is known only in certain widely scattered districts of the United States, including the upper and middle parts of the Mississippi Valley and the mountain regions of the Southern States.

Father Hennepin's accounts of his travels contain a reference to this disease among the cattle of the earlier settlers. But it was not until the first decades of the nineteenth century that it attracted much attention. The settlers in Ohio, Illinois, Indiana, and other States found that in certain localities there was a great mortality among cattle from a disease they called "trembles," and that the young of the affected cattle, and animals, or men fed on the flesh or milk of such cattle developed the disease. The distribution of the malady was very irregular and sharply limited to certain fields or pastures, usually wooded ridges which had never been cultivated. After clearing and cultivation the disease disappeared. Fencing off these pastures prevented the cattle from becoming infected. With the advance of civilization the infection grew less frequent, and by the time modern methods of investigation reached these localities the disease had almost ceased to exist.

To these factors of rarity and removal from centres of investigation are largely due our ignorance of its etiology. The best study of the malady is that of Graff,[1] who also did some experimental work. In fact, little has been added since his time. Way[2] contributes a good study of the disease in North Carolina in more recent times. In 1902, Collins reported 5 cases in Indiana with 2 deaths, while in 1904 four counties in Illinois reported 12 cases with 5 deaths. All these cases were definitely traced to "trembles" in the milch cows, and in one instance the death of two dogs from eating the cows' flesh is noted. They showed the typical symptoms of the disease.

The disease still occurs in thinly settled parts of North Carolina and East Tennessee. It is always difficult to trace on account of the reluctance of owners to admit that their herds are infected.

[1] *American Journal of the Medical Sciences*, N. S., vol. i, 1841, p. 351.
[2] *Ibid.*, vol. cvi, 1893, p. 307.

In a preliminary report, Hessler[1] (1905) describes the finding of a sterigmatocystis in the blood of a horse sick with the "trembles," and was able to cultivate the same on media. Experimental observations with these organisms are promised in a subsequent report.

**Etiology and Pathology.**—Many theories have been advanced as to the cause of the disease, among others mineral poisons in the soil or water, poisonous herbage, such as *Rhus toxicodendron*, mycotic infection, etc. Careful analysis of soil and water excluded the first, and inability to produce a disease communicable to other animals ruled out the second. The whole picture of the disease points rather to some living organism as the cause. Graff showed that infected milk, butter, or beef, which do not differ in appearance or taste from normal, produce typical and fatal attacks in dogs, and that the flesh of these latter was just as infectious as the original material. A litter of puppies suckled by an infected bitch all died of typical milk sickness. The virus, according to the same writer, was not destroyed by boiling. He was able to infect by the mouth only. No inoculation with blood, flesh, milk, or secretions was successful in his hands. Swine were immune. Slightly infected cows if carefully fed and kept quiet in a stall showed a sudden disappearance of the poison from the milk in about fourteen days. Graff's work is interesting and valuable, but is uncertain on the crucial point as to the inoculation of the disease, and cannot, therefore, be considered as settling the question as to intoxication or infection.

The disease is not confined to any time of year, but is more prevalent in the summer and fall, and apt to be more severe in dry years. The infected pastures are never increased in area, but seem rather to decrease with time. Areas formerly free have not been known to become infected. Clearing and cultivation, if persisted in, will render the pastures safe.

The pathological findings in fatal cases in cattle or in animals secondarily infected were the same: some injection with great contraction of the intestines and stomach, enlargement and softening of liver and spleen, while hemorrhages and exudation into the serous cavities were constant features. There was often great engorgement of the cerebral vessels, with some fibrinous exudation on the meninges and marked softening of the brain. The blood was usually quite fluid for a long time after death.

**Symptoms.**—In man the disease comes on after an incubation period of three to ten days, with languor, loss of appetite, and extreme constipation. Headache, tinnitus aurium, and muscular pains may be present in some epidemics and absent in others. There is great thirst, with nausea and persistent vomiting. In severe cases the vomitus is of a bile-tinged and soapy character and may contain blood. The tongue is swollen, flabby, shows the impress of the teeth, or may be protruded from the mouth and coated with a whitish fur. The breath has a peculiar, sweetish odor, which is quite characteristic. The pulse is quick, full, and soft, and the cases reported since the introduction of the clinical thermometer have been without fever or had only a very slight rise of temperature. The cerebral symptoms may be varied. Great irritability, convulsions, and marked delirium are characteristic of some epidemics, while in others drowsiness and coma are more common. The abdomen may be moderately distended and is doughy on palpation, and there is often marked epigastric pulsation. The urine is

[1] *Proceedings of the Indiana Academy of Science*, 1905, p. 122.

scanty, pale, and commonly shows a trace of albumin. In fatal cases death may occur in from three to ten days after the initial symptoms, coma and gradual cardiac failure being the terminal features.

The mortality varies greatly in different epidemics and may be from 10 to 90 per cent. The milder cases show a slow abatement of the symptoms, sometimes with critical discharges and a long convalescence. In this stage the slightest muscular exertion may bring on typical "trembles," as seen in cattle. Very often the patient is unable to work for months; others are more or less permanently incapacitated. Progressive dementia is said to have followed severe attacks in some instances.

**Diagnosis.**—In regions where "trembles" in cattle is prevalent, the recognition offers little difficulty, and in any case the occurrence of the characteristic nausea and vomiting, great thirst, enlarged tongue, and obstinate constipation without fever would make the diagnosis probable and lead to a careful investigation of the milk, butter, and meat supply. Cases are apt to occur simultaneously in families. Occasionally severe gastro-enteritis or a typical typhoid fever may be mistaken for milk sickness in regions where this prevails. The history and course of the disease should soon lead to a correct diagnosis.

**Treatment.**—There is little doubt that heroic bloodletting greatly increased the mortality in the days when milk sickness was very common. Absolute rest and free purgation, preferably with salines or castor oil, persistently administered until effective, gives excellent results. Stimulation with whisky or brandy is indicated in most cases. During convalescence strychnine, iron, and careful regulation of diet are advised. The patient must avoid severe muscular exertion for a long time lest he precipitate an attack of "trembles."

# PART II.

# DISEASES OF THE RESPIRATORY TRACT.

## CHAPTER XIV.

### THE MECHANICS OF RESPIRATION AND OF THE RESPIRATORY DISEASES.

By THOMAS R. BROWN, M.D.

**Introduction.**—In discussing the mechanics of respiration and respiratory diseases, the wisest course seems to review briefly the mechanism of physiological respiration in the light of recent investigations and follow this with as complete an exposition of the mechanics of the various pathological conditions of the respiratory tract as is possible in the limits of such an article, considering in the first place the various impediments to respiration, in the second place the effect such impediments have upon the respiration, and finally how and by what means the organism adapts itself to the new conditions.

#### ANATOMY AND PHYSIOLOGY OF THE RESPIRATORY TRACT.

It is advisable first to call attention to some points in the anatomy of the lungs before discussing respiration. The lungs may be considered as two large bags broken up into saccular divisions and subdivisions, finally consisting of little pouches or infundibula, the walls of which are hollowed out into alveoli. There are about 725,000,000 of these latter, varying from 120 to 380$\mu$ in diameter, and they expose a total air surface of about 200 square meters. These alveoli are bathed in about 1.5 kilograms of blood, so that we may consider the air cells as being surrounded by a film of blood 10$\mu$ in thickness. The right main bronchus is more nearly vertical than the left, and at the same time has a greater cross section, the relation of the right to the left being as 100 to 77.5. The first branches of the bronchial trunk are given off at right angles, and all the bronchi are hyparterial except one branch on the right side. On the right side the eparterial bronchus supplies the upper lobe, the first ventral hyparterial the middle lobe, and the other ventral and the dorsal hyparterial branches the lower lobe, while on the left side the first ventral hyparterial branch goes to the upper lobe, and all the

other branches to the lower lobe. A band of muscular fiber surrounds the opening of the terminal bronchiole into the atrium, but beyond this no muscle is found, according to Miller. Cilia are present almost to the terminal bronchioles. The terminal bronchiole has an average diameter of 0.4 mm., the atrium 0.28 mm., the air sac 0.41 mm. The entire volume of the bronchi amounts to between 100 and 120 ccm., while all the respiratory tissue amounts to more than 3,000 ccm. The trachea shows a peculiar variation in that it is smallest just below the larynx, from which point its cross-section steadily increases until about the middle of the tube, whence it again decreases to its termination, and this peculiar variation is repeated in the bronchi; by this mechanism the air is made to enter with a rotatory motion.

Most of the nerves of the lung originate from the anterior and posterior pulmonary plexuses; they contain both vagus and sympathetic fibers, the former belonging mainly to the musculature, the latter to the bloodvessels. The principal masses of lymph glands occupy the space between the right and left main bronchi, while single glands are found surrounding the bronchi and lying on the pulmonary artery.

Attention may be called to a few of the important facts regarding the physiology of respiration before discussing the mechanism of respiration under physiological and pathological conditions.

Regarding the frequency and depth of the respiratory movements, each of these is affected by many factors, such as age, posture, time of day, digestion, muscular activity, temperature, season of the year, barometric pressure, various emotions, the composition of the air and of the blood and the state of the respiratory centres and of the nerves. From 2,000 observations Hutchinson gives the rate as from 16 to 24 a minute for the average man, while Vierordt gives 11.9 and Ruef 19.35.

As to the rhythm of the respiratory movements the experiments made on Marey's pneumograph show, first, that inspiration passes into expiration without appreciable pause; second, that inspiration is shorter than expiration, the usual ratio being 5 to 6; and third, that the curves of inspiration and expiration differ in certain characters. It has been shown also that the inspiratory phase is relatively shorter in women and children and in the aged, that inspiration is more abrupt than expiration, and that there may be a pause between inspiration and expiration where the respirations are abnormally infrequent. It is also interesting to note that the respiratory rhythm, besides being affected by various pathological processes and emotional influences, is often disturbed in sleep, especially in the very young and very old; in fact, under these conditions we sometimes meet with typical Cheyne-Stokes respiration.

For the pressure conditions existing within the lungs and pleural cavity, slightly different figures are given by different investigators. Due to the fact that the lungs are in a state of permanent distension within an air-tight cavity, the intrathoracic pressure is always negative under normal conditions, this negative pressure being, of course, greater during inspiration, less during expiration, and also being somewhat affected by posture. Under forced expiration, however, where the air passages are obstructed, the intrathoracic pressure may become positive, as for instance during a violent coughing attack when there is obstruction to the expiratory blast. The intrapulmonary pressure, on the other hand, varies with the phase of the respiration, being negative during inspiration, positive during expiration.

As to the volume of air respired, the figures usually given are that the tidal air equals 500 cc., the complemental air 1,500 cc., the reserve or supplemental air 1,240 to 1,800 cc., the residual air 1,230 to 1,640 cc., and the stationary air 2,470 to 3,440 cc. The bronchial capacity is about 140 cc., while the alveolar capacity after quiet expiration equals from 2,000 to 3,000 cc., this, of course, being increased during inspiration and decreased during forced expiration. According to Vierordt, the vital capacity of the lungs—that is, the volume of air that can be expired after the most forceful inspiration averages in men 3,400 cc., in women 2,500 cc., and is affected by age, stature, sex, posture, occupation, and disease. The respiratory quotient also varies markedly with the food, age, time of day, temperature, muscular activity, composition of respired air, etc.

In the admixture and purification of air in the lungs three important factors are concerned: first, the tidal movements, due to inspiration and expiration, and acting by the mere force of the air currents; second, the cardiopneumonic movements, due to the heart beat; and third, the diffusion of oxygen and carbon dioxide, depending upon differences in the partial pressure of these two gases in the various portions of the respiratory tract. As regards the interchange of the two gases between the alveoli and the blood, the belief is general that this is due both to physical and to chemical factors, diffusion being the most important, although it may be possible that the living tissues play an active part in this process.

## THE MUSCULAR MECHANISM OF RESPIRATION.

To bring about the changes in the lungs which are known as inspiration and expiration, a mechanism is necessary to produce corresponding changes in the size of the thorax, for the lungs follow the thoracic movements because of the constant negative pressure in the pleural cavities and because of their perfect elasticity. Theoretically the thoracic movements might be brought about in any one of three ways: there might be an active inspiratory effort followed by passive expiration due to the elastic reaction of the thoracic and pulmonary tissues and to gravity, or there might be an active expiratory effort followed by a passive inspiration due to the relaxation of the expiratory muscles, or both inspiration and expiration might be active, due to the contraction of certain sets of muscles. In reality the first of these types of respiration, that is, active inspiration followed by passive expiration, is the method under normal physiological conditions. Due to the action of certain muscles, the thoracic cavity is increased in three dimensions: the lungs, because of the negative pressure in the pleural cavity and because of their perfect elasticity, follow the thorax; pressure within the lungs becomes less than the pressure of the atmospheric air; the air rushes in to equalize this difference in pressure and we have the act of inspiration. At the end of the inspiratory act, or a very short time afterward, the thoracic cavity decreases in the three dimensions, partly due to the relaxation of the inspiratory muscles, partly due to gravity, partly to the elastic reaction of the distended lungs, thoracic muscles and cartilages and abdominal muscles, and possibly partly to the action of certain expiratory muscles, although under normal conditions these play little if any part in the expiratory process; the lungs are decreased in size, pressure within them becomes greater than the atmos-

pheric pressure, the air is forced from the lungs to equalize this difference and we have expiration. According to some observers there is a distinct pause after expiration before the next inspiration is inaugurated, while according to others this pause is only present under abnormal conditions.

The chief muscles of inspiration, that is, the muscles which play the most important role in enlarging the thoracic cavity, are the diaphragm, the quadrati lumborum, serrati postici inferiores, scaleni, serrati postici superiores, levatores costarum, external intercostals and intercartilagines. The contraction of these muscles brings about an increase in the thoracic cavity in three dimensions by two processes, the elevation of the ribs and the descent of the diaphragm. The ribs show a double movement due to their articulation with the spinal column behind and with the sternum in front; they are elevated, the angle between them and the costal cartilage is straightened out, the sternum is pushed forward and upward and a slight rotation occurs so that the lower surface is turned slightly upward and outward. The elevation of the ribs also brings about an increase in the transverse diameter of the thorax, while the corresponding shortening of the vertical diameter is more than counteracted by the fixation of the lower ribs and the descent of the diaphragm. This elevation of the ribs is brought about by the contraction of a number of muscles of which the external intercostals are probably the most important, although the scaleni, the serrati postici superiores and the levatores costarum play a role in this process. These muscles raise the upper ribs toward the spinal column and fix them in this elevated position, the external intercostals raising all the ribs except the first and each intercostal acting from the rib above as a fixed point.

By the contraction of the muscular fibers of the diaphragm, first a lowering of the diaphragm and second a flattening of its circumference takes place, the latter being far the more important of the two under normal circumstances. On account of the attachment of the diaphragm to the six lower ribs the contraction of this muscle would tend to pull them inward, but this is counteracted normally by the simultaneous expansion of the rib cage due to the external intercostals and by the fixation of the lower ribs by the serrati postici inferiores and quadrati lumborum and by the lower portions of the sacrolumbalis. The contraction of the diaphragm may also cause a widening of the lower portion of the thorax by pressing on the abdominal viscera and thus extending the abdomen and pushing out the lower ribs.

As we have said before, quiet expiration is in all probability an absolutely passive process, although it is possible that the contraction of the internal intercostal muscles plays a part here; it is much more probable, however, that their chief function under these circumstances is to maintain the tension of the intercostal tissues.

Under pathological conditions, due either to obstruction to the entrance of air in any portion of the respiratory tract or to poor aëration of the blood due to any other cause, many other muscles are brought into play both during inspiration and expiration.

The accessory muscles of inspiration act mainly either by increasing the action of the inspiratory muscles described above or by furnishing them with more fixed supports from which to act. Thus the sterno-cleido-mastoid, the infra-hyoid, the pectorals, the trapezei and the rhomboidei muscles play an important role in labored respiration, aided further by the action of the

erectores spinæ in extending the spinal column and by the lower slips of the serratus magnus.

In forced expiration the most important muscles are those of the abdominal wall, which press upon the abdominal viscera, push the diaphragm upward, and pull down the sternum and ribs. In this depression of the lower ribs, the abdominal muscles are assisted by the serrati postici inferiores and by portions of the sacrolumbalis. The abdominal muscles also flex the thorax upon the pelvis and offer a base from which the internal intercostals may act, pulling the ribs downward, the triangulares sterni contracting at the same time and pulling downward the cartilages of the second, third, fourth, fifth and sixth ribs.

Under conditions of great obstruction to the inflow of air or in any case where the aëration of the blood is markedly hindered, and notably in severe cases of asphyxia, many other muscles may be called into play both in inspiration and expiration, in fact, every muscle that can depress or elevate the ribs, that can exert pressure on the abdominal viscera or that can furnish fixed points for either the inspiratory or expiratory muscles.

Due to the inspiratory change of shape and size of the thorax produced by the muscular mechanism described above and to the fact that the thorax increases more markedly in certain diameters (especially the vertical) than in others, there is a distinct movement of the lungs with respect to the thoracic cavity as it expands. This pulmonary movement takes place in two directions from two fixed points; vertically from the apex toward the base of the chest, so that during inspiration the lower border of the lung descends from the level of the sixth or seventh to that of the tenth or eleventh rib, and anteriorly from the mediastinal attachment of the lungs toward the front and the sides of the chest, so that the anterior margins of the lungs move forward and distinctly encroach on the cardiac dulness. This movement, of course, is rendered possible by the existence of a pleural cavity.

As regards the different types met with under normal circumstances, in men on quiet breathing the type is mainly diaphragmatic, the abdominal muscles and lower ribs being pushed out with each inspiration, while in women the costal type is met with in quiet breathing, the abdomen receding with each inspiration. According to most observers this difference in type is to be ascribed to difference in dress, as young children of both sexes as a rule have but one type of inspiration, the diaphragmatic. According to Mosso the thoracic type of breathing is frequently met with in males during sleep. In labored respiration, however, these differences between the diaphragmatic and costal types of respiration in the main disappear, and all the ordinary respiratory muscles and in many cases the accessory muscles are called into play, the set playing the greatest role depending upon the pathological conditions met with in the individual case.

Besides the respiratory muscles described above, certain other sets of muscles come into play, which, although they exert no influence upon the size or shape of the thorax either directly or indirectly, nevertheless facilitate the free entrance and exit of air to and from the lungs; most of these play an important role where the respiration is labored. The larynx shows an up-and-down movement even in quiet respiration, the upward movement corresponding to the expiratory phase, partly due to elastic reaction of the lung, partly to contraction of the thyro-hyoid muscles, while the depression of the larynx during inspiration is partly due to the contraction of the sterno-

hyoid and sterno-thyroid muscles, and partly to the deepening of the thoracic cavity and the consequent retraction of the trachea and lungs.

Under normal conditions there are but slight movements of the vocal cords, the *rima glottidis* being moderately open, but in deep breathing the contraction of the posterior crico-arytenoid muscles brings about a marked dilatation of the glottis with each inspiration.

The nostril is dilated with each inspiration, due to the action of the dilator naris, while during expiration the nostril is contracted, this being brought about mainly by the elastic reaction of the nasal cartilages, although possibly helped by the contraction of the compressor naris. These movements are more marked in children and are especially striking when there is marked obstruction to the entrance of air into the lungs.

## THE NERVOUS MECHANISM OF RESPIRATION.

In order to appreciate the mechanics of the respiratory diseases it is quite as important to have a knowledge of the nervous as of the muscular mechanism. The coördinated rhythmical contractions already described must be initiated in some portion of the central nervous system; in other words, there must be a definite respiratory centre. The exact position of the respiratory centre has been the subject of much physiological investigation. The motor cells of the cord which innervate the respiratory muscles, are called into activity either by nervous influences derived from afferent or sensory fibers or from fibers originating in cells of higher portions of the nervous system by way of the pyramidal tract fibers. Experiments have definitely shown that the spinal centres of their own accord are able to initiate the rhythmic respiratory movements, and that this higher centre is situated above the lower end of the medulla oblongata. Its exact position has been the subject of many experiments. Thus, Flourens believed that this centre was a small area just below the apex of the calamus scriptorius, of pinhead size and called by him the *noeud vital*, while according to Gierka the centre is situated in Krause's respiratory bundle, below and a little to the outside of the nuclei of the pneumogastric and glossopharyngeal nerves. Mislawsky places the nucleus in the formatio reticularis on each side of the median raphé, and Gad also believes that it is situated in this position. Although a number of observers have denied the existence of the respiratory centre, nevertheless the recent experiments are conclusive, and we may conclude with Starling that "for the normal performance and coördination of the respiratory movements, the integrity of certain parts of the medulla oblongata situated on each side of the median line is necessary, and that therefore these parts are the respiratory centre," although according to this same physiologist there is no experimental evidence of any anatomical separation between the expiratory and the inspiratory centres Reichert differs from this view and concludes that "each half of the respiratory centre may be supposed to consist of two distinct portions, one of which upon excitation gives rise to a contraction of the inspiratory muscles, the other to a contraction of the expiratory muscles," the former being also an accelerator, the latter an inhibitory centre.

The question of the presence of accessory respiratory centres in other portions of the brain or in the spinal cord will be discussed later, and we will

for the present confine ourselves to the two questions of fundamental importance regarding the medullary respiratory centre, first, the method of arousing the centre to activity, whether due to peripheral stimuli, changes in the cells of the respiratory centre, or changes of a physical or chemical nature in the blood or lymph, and second, the cause of the rhythm of this activity. According to Rosenthal the activity of the centre is automatic, although it is intimately dependent upon the condition of the blood, the discharges becoming more active if the free renewal of gases in the lung is obstructed in any way and becoming less active in the reverse condition, while Pflüger and Dohmen have shown that the respiratory centre may be stimulated either by a decrease of oxygen or an increase of carbon dioxide in the blood going to it. Pflüger's theory as regards the action of the respiratory centre is an interesting one. He believes that, due to the metabolic changes constantly going on in the cells of the centre, groups of molecules are produced possessing an affinity for oxygen in a very high degree, and that it is these reducing substances which act as the excitants in respiration. Fick and Golstein have shown the marked effects of variations in the temperature of the blood, while many observers have shown the influence of various afferent nerves upon the respiratory rhythm and activity.

It has also been shown that the centre can discharge rhythmically in the absence of any rhythmic afferent impulses, and therefore we may conclude that "the rhythmical discharges from the respiratory centre are due primarily to an inherent property of periodic activity of the nerve cells of this centre" (Reichert). Thus, the respiratory centre is so arranged that it can respond to constant stimulation by intermittent rhythmic discharges, and normally this constant stimulation may be derived from the afferent impulses reaching the centre, the venosity of the circulating blood, the metabolic changes in the nerve cells of the centre, while its response is also affected by stimuli from the volitional and emotional centres or portions of the brain. Thus the rhythm of the centre may be affected by a number of circumstances, by the will, by the emotions, by the composition, temperature and rate of supply of the blood and especially by certain afferent impulses, notably those originating in the vagus nerves.

**The Influence of Afferent Nerves on Respiration.**—This is of such importance that a brief review of some of the theories held regarding it is necessary. Of all the afferent nerves the vagi alone are the ones that play a permanently important role in this connection. According to Rosenthal "the cause of respiratory rhythm is to be sought in the existence of a resistance to the passage of impulses from the centre to the respiratory muscles, an increase of the resistance to discharge serving only to make each discharge more forcible, but the interval between consecutive discharges longer," while under normal conditions this resistance is diminished by tonic influences ascending from both lungs by the vagus nerves. According to Hering and Breuer the stimulation of the vagus is due to alternate contraction and expansion of the lungs, thus bringing about an automatic regulation of respiration, the expansion of the lungs sending inhibitory or expiratory impulses, its collapse sending inspiratory impulses up the vagi, thus exciting alternately activity of the expiratory and inspiratory centres. Most of the recent investigators oppose Rosenthal's views that the pneumogastric fibers in the lungs are purely inspiratory and call more and more attention to their expiratory functions.

Probably the most valuable work is that of Gad and of Head, because their experiments are practically free from the objections which might be raised in regard to the earlier investigations. Gad concludes that the only inpulses travelling up the vagi are expiratory or inhibitory in nature; that these impulses are excited by the condition of distension of the lungs and are therefore present even at the end of normal expiration, being abolished only by a total collapse of the lungs. On this theory, with every distension of the lungs beyond the normal, the normal inhibitory influence of the vagus is increased and we get an expiratory pause, while sudden collapse of the lung increases the inspiratory activity by bringing about a lessening of the normal inhibitory stimuli. Thus, as Head puts it, the vagi act like the governor of an engine in economizing the labor expended and in preventing the centre from wearing out by excessive exertion.

Meltzer opposes Gad's view that the vagus fibers in the lungs are purely expiratory or inhibitory and believes that this nerve contains two sets of fibers, the inspiratory and the inhibitory or expiratory, differing in their time relations so that when stimulated together the primary effect is expiratory, the more lasting effect inspiratory Although the vagus is the only afferent nerve of absolutely fundamental necessity for normal respiration, nevertheless many other afferent nerves have an influence on respiration; in fact, there are hardly any of these nerves the stimulation of which may not under certain circumstances bring about variations in the rhythm or in the activity of the respiratory centre. The most important of these are the inferior and superior laryngeal nerves (which are, after all, but branches of the vagus), the glossopharyngeal, the trigeminal and the cutaneous nerves.

Rosenthal's experiments have shown that stimulation of the central end of the superior laryngeal nerve has an almost purely expiratory effect, a weak current bringing about instant cessation of the inspiratory and expiratory pauses, a strong current bringing about strong contractions of the muscles of expiration. At the same time the swallowing centre is affected, bringing about elevation of the larynx and peristaltic contractions of the œsophagus. The object of this mechanism is, of course, to expel any foreign body which may reach the larynx or trachea.

Stimulation of the inferior laryngeal nerves frequently causes an inhibition of inspiration sometimes associated with active expiratory movements.

Excitation of the glossopharyngeal nerves brings about an arrest of respiration, the muscles remaining in the condition of contraction or relaxation in which they were when the stimulus was applied, and the stoppage lasting for about the time of the two or three preceding respirations. The object of this, of course, is to prevent the aspiration of food into the larynx.

An arrest of respiration may also be brought about by stimulation of the olfactory branches of the trigeminal nerve, notably by the inhalation of noxious or irritating gases, in some cases a pure expiratory reflex taking place.

The stimulation of a number of other nerves of the body produces various effects upon the respiratory apparatus. Thus, a gentle stimulation of most of the sensory nerves causes a quickening and increase in the inspiratory movements, while, if the stimulation is marked enough to produce pain, respiration is mainly of an active expiratory type. The application of gentle stimuli to any of the abdominal viscera or to the splanchnic nerves brings about either an increase in the expiratory pause or, more often, strong contraction of the expiratory muscles.

**The Innervation of the Lungs and of the Respiratory Muscles.**—The muscles moving the alæ nasi are innervated from the seventh nerve; those opening the glottis from the accessory portion of the vagus; the diaphragm is supplied by the phrenic nerves derived from the cervical cord by the fourth and fifth cervical nerves, while the intercostal muscles are innervated from the whole of the dorsal cord.

As to the innervation of the lungs, the nerves are derived from the pneumogastric, sympathetic and upper dorsal nerves, many small ganglia being scattered along their path. Roy and Brown have shown that among the pneumogastric fibers of the lung are to be found both broncho-constrictors and broncho-dilators, and their conclusions in regard to these fibers are: first, that the broncho-constriction and dilatation may be caused by stimulation of the peripheral ends of the vagus and each nerve supplies both kinds of fibres to both lungs; second, that the pneumogastric nerve contains both afferent constrictor and afferent dilator fibers; third, all efferent nerves pass through the pneumogastrics; fourth, asphyxia and inhalation of carbon dioxide cause broncho-constriction but not after section of the vagi; and fifth, that certain poisons affect one or the other of these two sets of fibers (as the paralyzing effects which atropine exerts upon the constrictor fibers). According to Bradford and Dean, the vagus possesses no efferent vasomotor fibers, but it does contain afferent pressor fibers The vagus in all probability supplies trophic fibers and secretory fibers for the mucous glands, while the sensory fibers for the trachea, larynx and lungs are also derived from this nerve. The sympathetic nerves supply trophic as well as efferent vasomotor fibers. According to some observers, however, there is no satisfactory evidence for assuming the existence of broncho-dilator fibers in the vagus.

It is of especial interest to understand thoroughly the innervation and the action of the bronchial muscle fibers because of the extreme importance of their contraction or dilatation in a number of pathological conditions, notably bronchial asthma and the various forms of bronchitis. A contraction of the smooth muscle fibers in the bronchi and bronchioles, whether large or small, has a threefold effect: first, a constriction of these tubes, second, a diminution of air space in the lungs, in other words a decrease in volume of the whole lungs provided no compensatory circulatory changes take place, and third, an increased resistance to the entrance and exit of air to and from the alveoli. The question of whether or not the vagus exerts a constant tonic action on the bronchioles is one which as yet cannot be answered satisfactorily. Chauveau has shown that section of the vagi in the horse brings about a disappearance of the vesicular respiratory murmur, which would tend to show that in this animal at least the vagus exerts a marked tonic action on the bronchial musculature. In dogs, on the other hand, this tonic action cannot be demonstrated under normal conditions, although it can easily be shown after the inhalation of air containing carbon dioxide gas in excess, the bronchi constricting slowly and the blood pressure rising.

**Accessory Respiratory Centres.**—The existence of a number of subsidiary respiratory centres both in the brain and the spinal cord has been claimed by a number of investigators, as a polypnœic centre in the *tuber cinereum*, an inspiratory or accelerator centre in the optic thalamus, an expiratory or inhibitory centre in the anterior, and an inspiratory or accelerator centre in the posterior corpora quadrigemina, and an inspiratory

or accelerator centre in the Pons varolii and the nuclei of the trigeminal nerves.

These centres in all probability do not act during normal respiration, but after section of the vagi experimentally or, in all probability, under a number of pathological conditions the respiratory centre can be regulated and controlled to a great extent by influences emanating from these so-called accessory centres.

## THE MECHANICS OF RESPIRATORY DISEASES AND PATHOLOGICAL CONDITIONS.

We shall attempt to discuss first as thoroughly as possible, although necessarily rather briefly, the mechanical conditions met with in the various respiratory diseases and the neuromuscular mechanism by means of which respiratory movements, differing from those met with under physiological conditions, are called into play, as well as the reasons for the especial type of respiration met with in the individual case.

The second subdivision will be devoted to a consideration of conditions which mechanically limit the excursions of the lungs, whether due to changes in the muscles, ligaments or bones of the thorax, or in the nerves supplying the respiratory muscles.

In the third subdivision the changes in the respiratory mechanism due to pathological conditions of the pulmonary circulation will be discussed, while the fourth subdivision will be devoted to a short consideration of the changes in the respiratory mechanism due to changes in the blood, to fever and to intoxications of various kinds.

The fifth subdivision will be devoted to a discussion of the changes brought about by variations in the composition of the respired air, both as regards variations in the amount of oxygen and carbon dioxide, and the effect of poisonous substances.

In the sixth and last subdivision we shall discuss in a general way dyspnœa and asphyxia, paying especial attention to the mechanical problems involved in these two conditions and also calling attention to certain peculiar types of respiration due to pathological changes in the respiratory centre itself.

## OBSTRUCTION AND NARROWING OF THE RESPIRATORY PASSAGES.

**Obstructions in the Upper Respiratory Tract.—Nose.**—Obstruction of the nasal passages may be brought about by a number of conditions, such as tumors, foreign bodies, fractures of the turbinate or nasal bones, hemorrhage, catarrh with thick secretions, hyperæmic conditions of the mucous membranes and adenoids in the nasopharynx. If but one side is affected no harm is done, because each nasal passage is sufficiently large to permit of the regular interchange of gases under normal conditions. If, on the other hand, there is a complete obstruction of both passages, mouth-breathing is produced, in which the adult, although first having the feeling of inability to breath properly, soon learns to regulate his respiratory movements so that even in eating there is no difficulty in respiration; in children,

on the other hand, very great dangers are present due to the possibility of their sucking milk or other foodstuffs into the larynx. Besides these mechanical effects, the nose under normal conditions acts as a filter, removing to a great extent the dust particles, bacteria, etc., in the respired air, so that, as F. Müller has shown, under normal conditions the contents of the alveoli and bronchi are sterile. In mouth-breathing, the air reaches the lungs in an unfiltered condition and at a lower temperature than under normal conditions.

As to the effect of nasal obstructions upon respiratory movements, the impediment is usually more marked in inspiration and a slower, deeper inspiratory movement is the most effective method of regulation.

**Pharynx.**—From the pharynx to the bifurcation of the trachea and the beginning of the bronchial system proper, we are dealing with the undivided portion of the air canal, and for that reason any obstruction even for a short period of time must prove extremely serious. In the pharynx itself, however, complete obstruction or even a marked degree of stenosis is comparatively rare. Such conditions may be met with where large pieces of food or other foreign bodies are caught in the pharynx, or in paralysis of the pharyngeal constrictors where a large mass is suddenly carried behind the velum, in the case of voluminous tumors, tonsillar swellings and retropharyngeal abscess.

**Larynx and Trachea.**—Stenosis of or obstruction in the larynx or trachea is of necessity far more dangerous than in any other portion of the respiratory tract because of its narrowness, especially in the region of the glottis, and because of its marked liability to the entrance of foreign bodies or to the production of various forms of swelling. Among the most important conditions are those producing pressure from without, such as glandular tuberculosis, mediastinal tumors, goitre, aneurism, etc., the impaction of foreign bodies in this portion of the tract, especially dangerous in cases of paralysis of the glottic closers, and various inflammations and swellings of the glottis itself, such as in diphtheria and œdema, various conditions of glottic spasm, such as pseudo-croup and asthma thymicum, paralysis of the glottic wideners, certain diseases of doubtful etiology, such as whooping cough, callous cicatrical contractions, which may be met with after wounds of various kinds, after operation, lupus and syphilis, and excessive granulation tissue formation, which is sometimes found after tracheotomy. All of these conditions bring about stenosis of the larynx or trachea to a greater or less extent according to the portion affected and the extent of the process, while in some conditions, notably diphtheria and œdema of the glottis, complete obstruction and closure may be produced.

Of peculiar interest are those forms of obstruction which act as an impediment to only one phase of respiration. Thus, in cases of a polyp with a long pedicle, or a flapping diphtheritic membrane situated below the glottis, we have an impediment acting only upon the expiratory phase, while an impediment to inspiration, which is far commoner, is met with in the ordinary cases of spasm of the glottis, in the cases of pediculated polyps or flapping membrane situated above the glottis, in œdema of the glottis where the swellings formed by the aryteno-epiglottidean folds lie in front of the rima during inspiration and in paralysis of the postici where the atonic cords are drawn together by the inspiratory effort.

In all these cases, whatever their cause, the most serious effects are found where the impediment is situated in the glottic region, as here is the narrowest

portion of the single air tube. Normally, the glottis is susceptible of extreme variations in width, its opening being controlled by the posterior crico-arytenoid muscles and its closing by the lateral crico-arytenoid, the thyro-arytenoid and the arytenoid muscles, all these muscles being supplied with twigs from the recurrent laryngeal branches of the vagus. During free normal respiration the rima glottidis stands widely open; for phonation the rima is closed posteriorly, while anteriorly a narrow slit is left open. Even in complete paralysis of the recurrent laryngeal nerves, respiration is not affected seriously, because, all these muscles controlling the vocal cords being paralyzed, the glottis remains immovably fixed with the cords separated by a tolerably widely-gaping fissure. In bilateral paralysis of the postici, however, the glottis forms a narrow slip, so that loud phonation is possible but the inspiratory phase of respiration is distinctly impeded.

**The Effect of Obstructions in the Upper Air Tract.**—The effect of all the above factors is the same in that either the entrance or the exit of the air is impeded or entirely obstructed, whether inspiration or expiration or both are effected and the degree of the obstruction depending upon the extent and location of the pathological process.

Of course, if complete obstruction exists for even a few minutes, death by asphyxia takes place. If, on the other hand, the lumen shows merely a narrowing or stenosis, the amount of air is diminished according to the size of the obstacle, and such a modification of respiration takes place that the needs of the organism are satisfied if possible; if the obstruction is of such an extent that regulation is not possible, death from slow suffocation will take place.

Obstructions to inspiration are more common than obstructions to expiration, and thus inspiratory is more common than expiratory dyspnœa. Observations in human beings have shown that the common mode of regulation in the case of obstruction to inspiration is a reduction in the number of inspirations, which at the same time become labored and deeper due to the calling into play of the accessory inspiratory muscles, and at the same time the diaphragm, scaleni and intercostals act more vigorously than under normal conditions. If the obstruction is very great the thorax pumps itself much emptier of air than under normal conditions and we thus have a drawing or sinking in of all the labile portions of the thorax, such as the jugulum, epigastrium, and the lateral, supraclavicular and subclavicular regions. Of course, the mechanical explanation of this is that the lungs are unable to follow the inspiratory changes of form of the thorax and therefore the atmospheric pressure can exert a much more marked effect. In severe grades of obstruction to inspiration the picture is a striking one, for all the accessory muscles are called into play; the larynx and trachea sink downward, the spinal column becomes straightened and the shoulders and arms are firmly planted to secure the utmost possible thoracic enlargement. Obviously, the effect upon the thorax itself will be more marked in those cases in which the thorax, especially its bony portion, is peculiarly labile; for that reason thoracic deformities are much more liable to occur in early life and especially if the resisting power of the bones has been markedly diminished as in rickets.

When, on the other hand, there is an obstruction to expiration, the inspiration is normal but expiration becomes slower and labored, the elasticity of the tissues not being sufficient to bring it about, and the accessory muscles

of expiration being called into play; the abdominal muscles contract vigorously, and the spinal column is bent forward in the effort to expel the air.

Thus, if the obstruction is to inspiration, we have a condition of inspiratory dyspnœa characterized by slower, prolonged and labored inspirations, the expirations being free and short, while in expiratory obstruction, inspiration is normal and expiration labored, prolonged and strengthened. If, on the other hand, there is an obstruction to both phases of respiration, as in croup, in severe cases of œdema of the glottis, where the swelling of the aryteno-epiglottidean folds is so great that it acts as a distinct impediment to inspiration as well as to expiration, in obstruction from large foreign bodies impacted in the rima, and in the case of cicatricial contractions and compression from without of high grade, the respiration is a combination of both the inspiratory and expiratory dyspnœic types, that is, both inspiration and expiration are labored, slowed and strengthened.

In all these cases of obstruction, if of high grade, the ordinary symptoms are varied from time to time by excessive attacks of dyspnœa, which are especially liable to be brought about by increased exertion of any kind. Also the special types of breathing, just described, may be substituted for a short time by a series of shallow, rapid respirations.

The rushing of the air through the narrowed portion of the tube produces a strident, rough or hissing sound, the so-called stridor, the intensity of which depends upon the degree of obstruction and the strength of the respiratory movement. As, usually, inspiration is most affected, the inspiratory stridor is generally more marked than the expiratory; other factors tending to make the inspiratory stridor more marked are the inspiratory traction of the trachea, which, not being followed by a free inflow of air, allows the outside pressure to act, and the fact that the velocity of the flow is, as a rule, greater during inspiration than during expiration. If, on the other hand, the obstruction is more marked during expiration, the abdominal muscles are called into play and the expiratory stridor becomes more marked than the inspiratory.

In all conditions where the vocal cords are no longer normally vibrated by the expiratory stream, as in inflammations, tumors, foreign bodies, destruction of portions of the cords or paralysis of the cords, hoarseness occurs and its degree may be used as a fair criterion of the extent of the pathological process, always remembering that we must take into consideration the general physical condition of the patient, because in cachexia or great weakness, the cords may have already lost their normal tone and the voice consequently become hoarse. This hoarseness may also be due to a paretic condition of the cords, which is sometimes produced by violent coughing, as in tuberculosis. An interesting type of voice, met with in conditions producing obstructions in the nasal passages or in the naso-pharynx, is the so-called nasal voice, which is due to changes in the resonant properties of the oral and nasal cavities consequent upon the obstruction. Thus, it is met with in cases of inflammatory swelling of the mucous membrane of the nose, polyps, adenoids and other new growths, and also in cases of paralysis of the soft palate, syphilitic destruction of the palate, cleft palate, etc., the tone of this type of voice being distinctly different in these two sets of causes, which is easily understood when we consider the differences in the existing mechanical conditions.

In all conditions causing hoarseness, if the pathological process is so extensive that the contractile ability is almost or entirely lost, aphonia or lack of voice may occur.

In all these changes in the voice the general condition of health and especially the condition of the thoracic organs plays an extremely important part. Good examples of this are the weak voice of those suffering with circulatory disturbances, the low broken voice met with in pleurisy and peritonitis, the toneless voice of patients with cholera, and the almost inaudible voice of the dying.

**The Explanation of the Regulatory Phenomena.**—It is obvious that in all these cases of obstruction, death would of necessity supervene within a shorter or longer period of time were it not for some form of increase of the respiratory activity which compensates for the disadvantages caused by the various forms of obstruction or impediment. We have already described what is the usual type of respiration met with in the various forms of obstruction to the inflow or outflow of air to or from the lungs when such obstructions are situated in the nose, pharynx, larynx, glottis or trachea. The physiological explanation of these various types of respiratory movements has long been sought for. Cohnheim showed that if an obstruction to inspiration was introduced into this portion of the respiratory tract in rabbits, the inspiration became prolonged and labored, while the expiration was normal, while if the obstruction were to expiration the reverse condition took place. It was first suggested that this deviation was brought about by the action of the blood upon the respiratory centre, for it has been definitely shown that when carbon dioxide is increased or oxygen diminished in the blood, the respiratory centre is vigorously excited and responds by an increased action of the respiratory muscles, whether this increase be in the frequency or in the depth of the respiratory movements depending entirely upon the cause of the dyspnœa in the individual case. It has been shown, however, that in the case of obstructions in the upper respiratory tract the change in the respiratory movements is noted before the change in the gaseous contents of the blood, and therefore we must seek for another explanation for this phenomenon. According to the experiments of Hering and Breuer, the explanation of these regulative respiratory movements is to be found in the self-steering ability of the vagus nerve. Each expansion of the lungs inhibits inspiration and furthers expiration, while each expiration has the opposite effect. Whether this is due to chemical influences, that is, the effect of the changed conditions of the air upon the vagus, or whether it is to be referred to the effect of changes of intrapulmonary or intrathoracic pressure upon the terminal fibers of this nerve, it is impossible at the present time to state definitely. Of course, it is essential to assume that the vagus contains both inspiratory and expiratory fibers, and certainly most of the recent physiological work seems to bear this out.

We have thus seen that any obstacle to either phase of respiration will tend to prolong it, and that the stimuli producing such a change in respiration must come through the vagus nerves. The value of this mechanism can be easily seen if these nerves are cut, for in such cases respiration is constantly dyspnœic. On the other hand, due to this regulatory mechanism, even more air is taken into the lungs than under normal condition, as Köhler has shown in rabbits (the reason for the increased consumption of oxygen being the increased activity of the respiratory muscles), and thus life may be prolonged,

metabolism maintained and nutrition preserved for long periods. In this reflex mechanism is to be found the cause of the respiratory conditions met with in the various stenoses of the upper respiratory tract.

**Obstructions Below the Bifurcation of the Bronchi.**—In considering the effect of obstruction below the bronchial bifurcation we must of necessity touch upon practically all the pathological conditions of the lungs and pleura because in these, pathological conditions are present which either directly or indirectly act as an obstruction to some portion of the bronchial or alveolar apparatus.

Below the bifurcation of the bronchi there are distinctly different mechanical conditions than above this point, for in the latter case there is a single-tubed apparatus, while in the former we have an increasing number of divisions of the air tube as we go from bifurcation to alveoli. For that reason, for any obstruction in the bronchial tree to act in the same way as an obstruction of the upper respiratory tract, all tubes of the same sectional area must be occluded to practically the same extent. Practically the only conditions which can bring about such a picture are general thickening of the bronchial tubes, general tetanic contraction of the bronchial musculature, and obstruction to each of the main bronchi synchronously. The first two of these conditions are met with in certain cases of bronchial catarrh, and much more commonly in emphysema and bronchial asthma.

If both the great bronchi are narrowed, due either to the presence of foreign bodies or to pressure from without, we have practically the same mechanical conditions as those met with in narrowing of the trachea or larynx, and the regulatory mechanism is of the same type; that is, the phase of respiration, which is impeded, becomes slower, deeper and more labored. If, on the other hand, only one of the two great bronchi is narrowed we have a distinctly different picture, and after the extremely rapid dyspnœic type of respiration, which is inevitable when the respiratory conditions are suddenly changed, we have comparatively slight changes in the respiratory mechanism, because of the adaptation to the new conditions and the fact that for ordinary demands one lung is amply sufficient. Whether we have a somewhat more rapid or a somewhat deeper type of respiration or both, depends upon the special conditions of the individual case. In fact, the self-steering of the regulatory mechanism has for its object the attainment of the best results under the existing conditions. It is extremely rare to meet with conditions which bring about a marked narrowing of the great bronchi, and it is only in case of foreign bodies, or pressure upon the bronchi by tumors or by aortic aneurisms that the lumen is sufficiently encroached upon to bring about impediments of appreciable moment to either phase of respiration. Obstructions or stenoses, whatever their origin, are of far more importance if the smaller bronchi or the bronchioles are affected, and in such cases the mechanical effects are much more harmful the narrower the bronchi and the weaker the musculature. For this reason such obstructions are more important in children, in old people, or in individuals with kypho-scoliosis than in healthy adults.

**Foreign Bodies.**—Obstruction due to foreign bodies is most likely to occur when a deep inspiration takes place during a meal, and thus it is peculiarly liable to occur when, with the mouth full, a person yawns, sobs, sighs or laughs. The foreign body is more likely to pass directly into a bronchus the deeper the inspiratory effort, and, due to the anatomical con-

ditions, the right side is more likely to be affected than the left. According to the shape and consistency of the body, partial or total occlusion of the main bronchus or of one of its branches may result, while it frequently occurs, sometimes after a considerable period of time, that after a severe attack of coughing the foreign body is transferred to another bronchial branch. In cases of stenosis of one of the chief bronchi, dyspnœa is always met with, but whether respiration is slower or more rapid depends upon the nature of the obstruction. Thus, if the impediment is of such a nature that a slowed, more labored form of respiration will affect the lung beyond the impediment, that type is inaugurated, while if the impediment is such that practically complete occlusion takes place, the sound lung alone must perform all the respiratory functions, and increased rapidity of respiration results.

The effect of local stenoses, whether due to foreign bodies or an interstitial sclerosis, secondary to the inflammation brought about by the inhalation of dust and dirt, or to ulcerations of various origin, syphilitic, tuberculous, etc., will be discussed after consideration of mechanical conditions existing in bronchitis. As to the question of congenitally occluded bronchi, Cohnheim believes that many cases described as such are in reality cicatricial contractions due to the causes just described.

**Bronchitis.**—The mechanical effects of bronchitis differ markedly according to the number and size of the bronchi affected, the amount and character of the secretion, and the available respiratory forces of the patient. Thus, in catarrhal inflammation of the larger bronchi the degree of narrowing is practically never sufficient to cause a marked hindrance to respiration, while, on the other hand, in inflammation of the smallest bronchi and bronchioles the hindrance to respiration may be of extreme moment; obviously such a hindrance will be of much greater significance in children, where the air-tubes are smaller and the muscular power weaker, and in the aged and feeble than in adults in a normal state of health. Thus, in bronchitis there are all grades of dyspnœa, reaching, in the case of marked obstruction in the bronchioles of a large portion of the pulmonary tissue, a degree not surpassed by any other respiratory disease.

As to the type of respiration in bronchitis, this is obviously very different according to the conditions in the individual case. Thus, if we have practically the same degree of narrowing in all bronchi of the same calibre, there is a mechanical condition closely simulating narrowing of the trachea or larynx, and the best way of overcoming such a condition is by a slower, more forceful series of inspirations and expirations; as we shall see later, however, expiration is more likely to be prolonged than in tracheal or laryngeal stenosis. In most cases of bronchitis there is simply an increased frequency of respiration. The exact cause of this is still unexplained, part of it being referable to the fever usually present, while, according to Traube, most of this quickening is referable to the stimulation by the inflammation of certain fibers of the vagus nerve. On the other hand, in certain cases of bronchitis affecting a large area where the closure of the small bronchi and bronchioles is incomplete, as for instance in a diffuse, dry bronchitis of moderately small bronchi, a considerable amount of air may reach the lungs through the affected bronchi, and for that reason the best regulation is obtained by inspirations that are deeper than normal and not too quick; in some rare cases there is even distinct slowing of the respiratory rhythm. In

chronic bronchitis other conditions play a role; thus, we must also take into account atony of the bronchial muscles, loss of elasticity, and lack of contractile power due partly to the effect of the inflammation upon bronchial musculature and elastic fibers, and partly to the increased expiratory pressure, which is, of course, especially marked during paroxysms of coughing.

The prolongation of expiration so commonly met with in bronchitis is easily explained, being due to the fact that during expiration the contraction of the elastic thorax tends to still further contract the already stenosed bronchioles, and thus render the exit of air more difficult, which is increased if the abdominal and other accessory muscles are called into play.

Thus, in bronchitis we may meet all possible types of respiration extending from a simple increase of frequency on the one hand to a slower, more labored respiration with an especial lengthening of the expiratory phase and a marked expiratory stridor on the other hand.

**Effect of Local Stenoses of the Bronchi.**—These are due in the majority of cases to various forms of inflammation but occasionally to the presence of foreign bodies, and as there is no bronchial anastomosis, the area beyond the obstruction, if complete, is lost to respiration, and therefore we have a corresponding diminution of the respiratory surface. If the stenosis or obstruction affects only a moderate proportion of the bronchi the loss is easily supported, as the respiratory surface is constituted to meet the most sudden demands for oxygen. In other cases the obstruction reaches such a grade that breathlessness occurs, and the dyspnœic respiration met with in such cases, the deep inspirations and the forced expirations, is in many cases sufficient to overcome or remove the obstacle.

It is interesting to consider the effect of total occlusion or stenosis upon the portion of the lungs supplied by the involved bronchi. Of course, in cases of total occlusion of a large bronchial territory the whole force of the inspiratory pull is exerted upon the pervious sections of the lungs. Experiments on rabbits show that if one main bronchus is tied, death occurs either from rupture of the other lung and pneumothorax, or because of the stasis of the blood in the abnormally dilated pulmonary vessels. If less lung tissue is cut off, however, it has been shown that a true compensatory hypertrophy takes place, the actual increase in growth being brought about by the increased circulation in the unaffected portion of the lungs. When a comparatively small portion of the pulmonary tissue is involved the compensatory dilatation and hypertrophy is largely confined to the contiguous portions. In those portions undergoing this so-called vicarious emphysema it is generally only the bronchioles with their thin and yielding walls that take part in this compensatory dilatation, and the larger bronchi escape if nothing is present to prevent dilatation of the alveoli. On the other hand, if the walls of the bronchi have been weakened by inflammations of any kind we may find a dilatation of the bronchi of medium size.

Not less interesting is the effect of total occlusion of the bronchus upon the portion of the lung lying beyond it In this, complete atelectasis occurs, the air being absorbed by the circulating blood. This is rendered possible by the vicarious dilatation of the alveoli occupying the neighboring pervious section of the lungs, for by this means the tension of the confined air never falls below the degree necessary to absorption. In the atelectatic portion of the lung the circulation continues, and we therefore may meet with products

of transudation or exudation, while the small bronchi do not of necessity stop secreting, and if this secretion is abundant we may find a condition of bronchiectasis; although some observers deny the possibility of this, the experiments of Lichtheim have shown that it is possible.

If, on the other hand, the bronchus is not totally occluded, but only narrowed, a different picture is presented. In cases of obstruction within the thoracic cage the expiratory efforts tend to distinctly increase this obstruction, and, in fact, in marked cases to convert an obstruction into a complete occlusion, while as a rule the inspiratory effort lessens the degree of the obstruction. For this reason we have a condition in which more air enters than leaves the portion of the lung lying beyond the occlusion, and thus we have dilatation of the alveoli becoming more and more marked, which may in time lead to a true emphysema, generally of the vesicular, but in extreme cases, of the interstitial type. In the vast majority it is when the smaller bronchi are affected that such a condition is likely to occur, and for that reason emphysema is met with peculiarly frequently in bronchial asthma and in *catarrhe sec* in which the medium-sized and small bronchi are affected.

**Bronchial Asthma.**—There is no better example of a general bronchial stenosis than this. There has been much discussion as to its exact nature; the best explanation is that it is due to a tetanic contraction of the small bronchi, and that it is more a neurosis than a true inflammation. In many cases it seems to originate reflexly from various portions of the body, especially the nose.

From the hindrance to inspiration and the much greater hindrance to expiration, there is a combination of both the inspiratory and expiratory types of dyspnœa, the latter being much more marked and in its manifestations calling into play all the accessory muscles of expiration. During the attack, the volume of the lungs markedly increases in size, due to the greater obstruction to expiration, while a deep inspiratory sinking in of the soft parts also occurs. The patient is cyanotic, and the number of respirations may be normal, increased or decreased. Although at the conclusion of the paroxysm the lung resumes its normal condition, nevertheless the strain upon the pulmonary tissues is so great that after a shorter or longer period we are likely to meet with various forms of bronchitis and emphysema. This same form of paroxysmal dyspnœa is often met with in old cases of emphysema and bronchial catarrh; in these it is certain that the condition is also due to a spasm of the bronchial musculature, set up reflexly from the inflamed mucous membrane

**Emphysema.**—In emphysema the lung tends to constantly approximate its inspiratory condition with slight excursions during inspiration and expiration, while if many septa are destroyed there is also a real loss of respiratory surface. Therefore in pure uncomplicated emphysema respiration is likely to be shallow and hastened, with slight disturbances during rest but marked during exertions of any kind. In many cases of emphysema, however, we have an associated bronchitis, especially a diffuse dry bronchitis of the smaller tubes, and this is likely to modify the respiratory picture; if the inflammation is such as to produce a partial stenosis of a large proportion of the bronchi we may have a diminished rate of respiration with marked prolongation of the expiratory phase. Thus, the respiratory picture varies markedly according to the factors involved, for we are dealing with a condition associated with a loss of pulmonary elasticity, with diminished elastic-

ity of the thorax, often diminished strength of the respiratory muscles, and very frequently also with a bronchial stenosis of greater or less extent, and the type of respiration met with in the individual case is that which is best designed to overcome the especial respiratory hindrances. According to Sahli, the type met with may be described as prolonged expiration with expiratory stridor, characterized also by a greater or less tendency to quickening, although we may have slowing of respiration or a normal rate.

**Pneumonia.**—In pneumonia the type of respiration is partly due to the diminution of respiratory surface, partly to the mechanical limitations of the lungs' excursions, partly to the commonly associated pleurisy, which renders deep excursions painful, and partly to the effect of the increased temperature and of the toxins upon the respiratory centre. We usually, of course, meet with a shallower, more rapid respiration, the extent of these disturbances being dependent upon the extent of consolidation, the amount of normal air space remaining, the rapidity of the process, the demands of the gaseous exchange, and the physical condition of the different parts of of the compensating respiratory mechanism.

**In œdema of the lungs, hemorrhagic infarct and pulmonary hemorrhage** the mechanical conditions are practically the same as in pneumonia, except that, as a rule, we do not see the effect of the increased temperature or toxæmia. In these it is simply a case of how many alveoli are lost to respiration and how much the free movements of the lungs are inhibited.

**Tumors.**—We meet with a number of conditions which affect respiration, partly by pressure, partly by destruction of a certain amount of air space. Among these may be mentioned aneurism of the aorta or of the pulmonary artery, mediastinal tumors, swollen bronchial glands, epithelioma of the œsophagus, metastatic nodules in the bronchi or lungs, mycotic foci, and tuberculous consolidations. In all these cases the character or origin of the growth is immaterial, and also whether it renders the alveoli impervious by penetration or by compression. The respiratory phenomena met with depend upon the amount of lung tissue thrown out of function, the degree of inhibition of free movements of the lungs produced by the pathological condition, and whether or not the process is one which is associated with fever and toxæmia.

**Bronchiectasis.**—In bronchiectasis the dilatation must occur at the expense of a certain number of alveoli, as the thorax is a closed cavity. Thus the respiratory picture is partly dependent upon the consequent diminution of respiratory surface, partly upon the frequently associated bronchitis.

**Pleural Effusion.**—The question of the mechanics of pleural effusion is extremely interesting and has been the source of much discussion. According to the usual view, in the first place, the lung is compressed with a consequent diminution of respiratory surface; in the second place, we have a mechanical limitation of the lungs' excursion, while if the effusion is great we may have a compression of the sound lung as well as a limitation of its movement; in the third place, due to the lessening or lack of negative pressure, we may have less or no aspiration of venous blood, while the pressure of the exudate on the veins in the thoracic cavity may exert a marked effect upon the right heart.

Garland, who has performed a very interesting series of experiments upon the mechanics of pleural effusions, and who was the first to especially insist upon the so-called *S* curve of the lower limit of the effusion, differs quite

markedly from most writers as to the dynamics of pleural effusion. His work is of such importance that it will be well worth while to summarize his conclusions as follows:

1. That the letter *S* curve can be traced only in the erect position, and when the play of the lung is not hampered by adhesions; and that its persistence throughout the various stages of an effusion indicates the absence of adhesions in the lower part of the chest.

2. That the letter *S* curve of flatness corresponds in shape to the lower border of the lung, and in position to the line of apposition between the lower border of the lung and the upper border of the effusion.

3. That the letter *S* curve is pathognomonic of a fluid effusion in the pleural cavity, but that it is impossible to judge from any variations in the curve as to the nature of the fluid present.

4. That an effusion does not immediately intrude between the lung and the lateral chest wall, but that such intrusion occurs last of all, whatever be the position of the patient.

5. That a pleuritic exudation does not compress the lung in the manner universally taught, but that, on the contrary, the effusion exerts a *negative pressure* by virtue of its weight.

6. That the lower part of the lung does not become first compressed and then plunged into the fluid beneath, but that the entire lung contracts symmetrically throughout.

7. That the lung does not, properly speaking, swim upon an effusion, but that, by virtue of its retractility, it supports the entire body of the effusion, together with the diaphragm, until the weight of the fluid exceeds the lifting force of the lung.

8. That the position and shape which the lung assumes when associated with an effusion are determined by the balance between the weight of the fluid and the elasticity of the lung.

9. That the position and shape which the effusion assumes are determined by the varying degrees of retractility in different parts of the lung, and by the position of the patient, complications being left out of consideration.

10. That the excess of weight of an effusion is free to act upon the diaphragm according to its specific gravity.

11. That the diaphragm does not bag down until the weight of the effusion exceeds the lifting force of the lung, and the same holds good for obliteration of the intercostal depression.

12. That the heart, mediastinum, etc., are not pushed out of place by an effusion, whether of air or fluid, but that those parts are drawn over by the opposing lung. Enormous effusions may, of course, increase the displacement.

The mechanical conditions met with in pleural effusion are usually explained mainly from a consideration of the pressure conditions within the lungs and within the pleural cavities, the intrinsic elasticity of the lungs and thorax, and the effect of gravity. These influences cause, first, the accumulation of fluid in the dependent portions of the thorax, which in its turn brings about a relaxation of the diaphragm and a consequent diminution of the downward action of this muscle; in other words, the respiratory excursions of the lung and diaphragm diminish as the exudate increases. According to Rosenbach, another and more important influence is at work, which he describes as tonus. He regards the diaphragmatic displacement as third

in the chain of events associated with the exudate, these being, in order, a certain dilatation of the thoracic space, due to relaxation of the muscle tonus, a secondary compensatory diminution of that portion of the lung particularly affected, and downward displacement of the diaphragm with its associated dislocation of the abdominal organs.

The conclusions of Garland seem to give a far more satisfactory explanation of the mechanics of pleural effusion than those suggested by any other writer on the subject.

**Pneumothorax.**—In pneumothorax the study of the mechanical conditions is as interesting as in pleural effusion. We have to consider the mechanical effects both in open pneumothorax, where there is a positive pressure in the pleural cavity, and of closed pneumothorax, where the normal negative pressure is diminished or where the pressure may even be positive, although to not so great an extent as in closed pneumothorax. In closed pneumothorax when air is present and does not vary much with inspiration and expiration, respiration is not prevented, and we have practically the same conditions as those met with in pleural effusion. If, however, the opening is of a valve-like nature the air may possess abnormally high tension, so that finally the affected half of the thorax is expanded to a greater extent than that met with even in the deepest inspiration, and in these cases the lung is not only airless but compressed. In open pneumothorax, whether it be due to a perforating wound, a fistula, the rupture of a tuberculous or a bronchiectatic cavity, abscess, a focus of gangrene, or an emphysematous vesicle, or, as is much less often the case, the perforation of an œsophageal or gastric ulcer, the lung is able no longer to follow the inspiratory pull of the chest wall, little or no air enters, and atelectasis to a greater or less extent results, although, of course, if pleural adhesions are present the pneumothorax is saccular, and the atelectasis partial. Both types of pneumothorax cause, to a greater or less extent, diminution of the respiratory surface and a mechanical limitation of the lungs' excursion.

According to Rosenbach the pathogenesis of pneumothorax is not so simple as to be explainable solely on mechanical grounds; in fact, according to him, the nature of the fistulous opening, on which a special subdivision into open and closed valvular pneumothorax has been based, is of less importance than the condition of the respiratory apparatus itself. Thus, maintenance of the normal pressure relations will depend upon the size of the opening, the rigidity of the walls, the elasticity of the lung tissue in the immediate vicinity of the opening, and the irritability of the reflex apparatus. Obviously, if there is a direct communication between a large bronchus and the site of perforation, or when a small rigid bronchus gapes at the surface of the pleura, this mechanism or tonus, on which Rosenbach lays such stress, cannot act, as it is insisted by this investigator that the pulmonary tissue is under the influence of an active tonus, and the inspiratory expansion does not depend so much on the difference between the internal and external air-pressure as on the relaxation of this tonus, a view, by the way, which is opposed by most investigators in this field. Rosenbach considers that the greater the loss of elasticity in the diseased lung, the greater the accumulation of air within the pleural cavity; thus it is greatest in tuberculous and other diffuse infiltrations of the pulmonary parenchyma, and least in those cases of pneumothorax occurring in practically normal lung tissue. In this latter case, that is, if the lung tissue is healthy, under favorable conditions

the fistula must, owing to the "affinity of the tissues," eventually become closed by the vicarious activity of neighboring parts; that is, the inflation brought about by the necessary relaxation of the tonus, and the adaptation of the parts, effects a kind of tamponade about the fistula, diminishing the movements of air in that region to such an extent that the healing process has a chance to begin.

The most complete review of the whole subject of pneumothorax including the mechanics of this condition is to be found in the monograph of Emerson.[1] According to the vast majority of observers, the tonicity of the lung has no influence on its elastic tension, although West, like Rosenbach, lays great stress upon this as a factor. As to the exact amount of the negative tension it might be well to mention here the figures of Cane and Aron on a normal living person. During quiet inspiration an average of −4.65 was obtained during quiet inspiration, and −3.02 mm. Hg. at the end of expiration. As to the question of whether or not there is a cohesion between the layers of the pleura, there is much difference of opinion. Auquier, Dolbeau and Smith, West and Piqué believe that there is a real cohesion between the two layers of pleura, this, according to West, amounting to 12 mm. of mercury. Northrup, on the other hand, was unable to demonstrate this, and in Emerson's experiments no such cohesion could be demonstrated. To quote from this latter investigator, "when air is allowed to enter the pleural cavity the lung begins to collapse. If the perforation be a parietal one and the diameter of the opening be less than that of the bronchus to that lung, the air will enter with each inspiration, and during expiration some of the lesser amount be expelled, until the lung at the end of expiration is just collapsed. Then with each succeeding breath the lung will expand somewhat with each inspiration, since more air can enter through the bronchus to fill the partial vacuum than through the perforation. With each expiration the lung will assume its former collapsed condition, since the air escapes more easily from the bronchus. The smaller the hole the greater the expansion of the lung, and in case it be then closed the lung can take no small part in respiration." This is practically the same description as that given by Bell, who likened the thorax to a pair of bellows, and regarded the lung as being moved by the vacuum. According to Garland, the air, if it enters at the base, remains there until the base has ascended some little distance; most observers do not believe that the lower lobe becomes airless first, but that the lung collapses as a whole. Sehrwald insists upon the importance of the condition of the mediastinum as regards the sound lung, showing that the more it is stiffened the less the effect of pneumothorax upon the sound side.

As regards the mechanics of the valvular form of pneumothorax, according to Weil the air enters during inspiration, while according to Bouveret it is the violent expiratory effort of coughing that forces air into the pleural cavity; according to Bard, coughing forces the air from the pleural cavity, and the positive tension met with in valvular pneumothorax is due to the regular play of the respiratory movements and is equal to the normal pulmonary tension. We have already spoken of the limitation of movement, which takes place in the other lung, this being greater, the more normal the mediastinum, that is, the less it is pathologically thickened.

[1] *Johns Hopkins Hospital Reports*, vol xi.

As to the respiratory phenomena met with in pneumothorax, various investigators report slightly different observations. Gilbert and Roger found that the respiratory rhythm at the onset of pneumothorax was greatly disturbed, marked inspiratory efforts lasting for a short time, after the condition was well established in open pneumothorax the rate becoming faster, the inspirations deeper, while in closed the rate became slower and inspiration slightly deeper, though not to the same extent as in open pneumothorax; in a closed double pneumothorax the rate increased, the amplitude diminished. According to Krebs, the excursions increased both in rapidity and depth in open pneumothorax, the increase of the rate varying directly with the diameter of the fistula, while Blumenthal found the rate increased in all forms, the volume breathed in the unit of time increased in closed, and diminished in open pneumothorax, the diminution varying inversely as the diameter of the fistula, while the depth was diminished in all forms, in the open form depending upon the size of the fistula. Sackuer found that the increased rate immediately after the formation of an open pneumothorax enables one lung to do the work of both. According to Aron's experiments "the result of a partially forming (valvular) pneumothorax is more frequent and superficial respirations, the chest expanding more forcibly, the diaphragm descending. The breathing movements then increase to a maximum in depth. In closed cases on the sound side the tension becomes even more negative, the movements are deeper and slower."

**Other Conditions.**—There are numberless other conditions which affect the respiratory mechanism, either by diminishing the respiratory surface or by inhibiting the respiratory movements to a greater or less extent. No condition is more important in this connection than *adhesion of the two layers of the pleura.* Normally, of course, the lungs increase in volume not only in transverse and anteroposterior diameters but also vertically, so that during inspiration there is a distinct movement of the lungs in regard to the thoracic cavity, this movement being from behind forward, and from above downward, the apices and the posterior margins thus participating least in the change of position, while the displacement of the inferior margin of the lungs may be taken as the best measure of the expansile power of the alveoli collectively. If adhesions occur between the two layers of pleura the expansion of the lungs will be affected; the effect will, of course, be least if the adhesions are at the apex or the posterior portions of the lungs while it will be greatest if they are met with along the inferior margins.

Among the other conditions which affect respiration either by diminishing the air space or making the respiratory movements less free, may be mentioned large tumors within the thorax, enlargement of the heart and pericardial effusions, aneurism of the aorta, substernal goitres, hypertrophy of the thymus, mediastinal tumors, the forcing upward of the diaphragm by abdominal tumors, ascites or meteorism, and thoracic deformities, especially kypho-scoliosis, in which that half of the thorax toward which the convexity of the spinal curve is directed may occasionally be much reduced; all these prevent the affected lung from expanding in a normal manner. The change in the character of respiration, which is met with, will be discussed later and here we simply call attention to the fact that although deeper inspirations can compensate if the compression is moderate, this is extremely difficult to keep up for long periods of time, and some other method than a simple deepening of inspiration is usually inaugurated. As

to the portion of the lung most affected by these various conditions, that, of course, entirely depends upon the processes themselves; thus, in the case of meteorism, ascites and abdominal tumors, it is the base of the lung; in pericardial effusion, mainly the inner portion of the left lung; in mediastinal tumors, the anterior borders of the lungs, and in substernal goitre and thymic hypertrophy the anterior portion of the upper lobes.

Although the lung may regain its normal state when the causative factors are removed, nevertheless, in a number of cases the compression is either so great or of such long duration that diminished elasticity of the pulmonary tissue results, which, of course, must act prejudicially on the expiratory contraction of the alveoli; thus, any strong compression of the lung and also abnormal vicarious inflation must exert an injurious effect upon its elasticity, especially if the condition develops rapidly and lasts a long time, this being the explanation for the condition of local atelectasis or of local emphysema frequently met with in such cases.

**The Effect of the Preceding Conditions upon the Respiratory Mechanism.**—The effect of these various diseases is to lessen the respiratory surface to a greater or less extent, and diminish more or less the ability of the lung to expand in regular fashion. The type of respiration met with depends not only on these two factors, but upon a number of others, among which may be mentioned whether the pathological process is local or general and its extent, whether the air spaces are entirely obliterated in the affected portions of the lungs or only partially encroached upon, whether the process is rapid or slow in development, whether or not it is associated with pyrexia or toxæmia. The condition of the neuromuscular respiratory mechanism, and of the pulmonary tissues, especially as regards their elasticity, that is, the compensating help of the respiratory movements, and the demands of the gaseous exchange must be considered. Thus, in determining the type of respiration met with, we have to consider many factors besides those definitely referable to the pathological process itself, such as the age of the patient, the functional condition of the respiratory bones and muscles, the condition of the patient's nervous system and of his various organs, notably, of course, the heart and the kidneys, his ability to have the proper amount of rest, fresh air, etc. Generally speaking, the organism accommodates itself better to a definite loss of respiratory surface, the slower the development of the pathological process on which this loss depends. If the loss of alveoli takes place very rapidly the respiratory symptoms are much more marked, as in the stormy symptoms met with in lobar pneumonia, acute miliary tuberculosis, pneumothorax and acute pulmonary œdema. Generally speaking the respiratory disturbances are greater the greater the diminution of the respiratory surface, if the demand for oxygen remains the same. If fever is present there is a tendency to increased frequency, that is, a heat tachypnœa, in addition to the effects of the pathological process itself, this increased temperature, of course, bringing about an increased production of carbon dioxide, and an increased pulse rate with a consequent greater demand for oxygen.

The exact type of respiration met with in the individual condition varies very markedly, as it depends upon all the factors mentioned above. Nevertheless, in every case it is in all probability the best type of respiration to overcome the pathological conditions presented. Thus, we may have an increased rapidity of respiration, or an increased depth of respiration, or a

combination of these two, or we may meet with a shallow quickened respiration, or a slower deepened respiration. Increased frequency of respiration is very common, especially in association with fever, when deep respirations cause pain as in acute pleurisy and peritonitis, in cases where large portions of the lungs are positively prevented from expanding and where the increased rapidity is referable to an irritation of the vagus endings, as in bronchitis. In many cases of diminution of the respiratory surface a deeper respiration is frequently met with, especially when the affected air cells are not entirely obliterated. In emphysema, open pneumothorax, especially if bilateral, and in other conditions in which rapid expansion or contraction is difficult, due either to changed pressure relations in the pleural cavities, diminished elasticity of the pulmonary tissue, or impediments to either inspiration or expiration affecting a large portion of the lungs, a respiration slower than normal may be met with, and we may have either an inspiratory or expiratory dyspnœa or a combination of the two. On the other hand, a very superficial shallow type of respiration is frequently seen, where deep inspirations would cause pain, as in pleurisy and peritonitis.

Generally speaking, increased rapidity of respiration with a tendency to increased depth is the respiratory type most frequently met with. Although in certain conditions, such as general pulmonary œdema and bilateral pneumothorax, death occurs unless the condition passes off rapidly, nevertheless in most of the conditions described the type of respiration inaugurated is able to compensate for the respiratory deficiency due to the pathological process itself, and the dyspnœic form of respiration is a means of compensation of the most efficient and helpful kind. Practical experience shows that by this means the functions necessary to life may be carried on satisfactorily, if not perfectly, while numerous experiments show that the gaseous exchange under the pathological conditions may be even greater than under normal conditions. Thus, Weil and Thoma showed that in closed pneumothorax in rabbits the quantity of air inspired during the unit of time was actually increased, while Möller showed by means of Pettenkofer's apparatus that in patients with pulmonary disease the exchange of gases does not differ essentially from that in normal persons, a result which is borne out by daily experience. Although in all cases the dyspnœic respiration is the most efficient means of compensation, nevertheless it must be remembered, in the first place, that there is a limit beyond which compensation is impossible, and, in the second place, that in all cases internal respiration is affected to a greater or less extent. In serious conditions where compensation is imperfect we can diminish as far as possible the demands for oxygen by absolute rest and by preventing anything which will act as an impediment to the compensating mechanism; thus the patients may lie upon the affected side in cases of unilateral hindrances to respiration, while in many cases the upright position renders respiration easier by facilitating the action of the auxiliary respiratory muscles, by removing or at least lessening the pressure on the diaphragm from the abdominal organs and by facilitating the flow of blood in the cerebral veins.

## THE PROTECTIVE MECHANISM OF THE LUNGS.

Two matters of extreme importance require mention: first, the protective mechanism of the lungs, and second, the means by which foreign bodies are removed from the air passages. The air passages may be regarded as a long, narrow, protected tube system, in various portions of which special mechanisms are introduced to prevent the entrance of foreign bodies into the deeper portions. The various mechanisms are so efficacious that, according to F. Müller, the contents of the alveoli, and of the bronchi, even as far as the trachea, are sterile under physiological conditions. While this is mainly due to the protective mechanisms, nevertheless it is helped by the fact that in the bronchial tree the air does not move violently, diffusion being far more important than the tidal movements, so that dust and bacteria, if present, settle on the mucus which coats the mucous membrane in a thin layer, and is then gotten rid of, the length, narrowness and tortuosity of the air passages aiding greatly in this process.

The first of these protective mechanisms is the mucous membranes of the nose, for on the folds and elevations, produced by the turbinate bones, a large proportion of the foreign material is deposited, as shown by the enormous increase of such bodies in the lungs when the turbinate bones are destroyed, or the nasal septum is affected. The epiglottis is in reality of less use than usually supposed, as shown by the fact that absolute paralysis of the depressors of the epiglottis, as in diphtheria and bulbar paralysis, or complete absence of the epiglottis, as met with in tuberculosis or syphilis, is without danger if the glottis is normal. In normal deglutition the root of the tongue is so placed in front of and above the entrance to the larynx that it is able to close the aperture without the aid of the epiglottis, which is substantiated by experiments performed on animals, which show that after swallowing colored dyes the epiglottis is unstained, and also that after the extirpation of the epiglottis little food enters the larynx. The most important protective mechanism is the glottis, and in persons with vocal cords intact, with the glottic closers functioning properly, and with normal sensibility of the glottic mucous membrane, the danger of the passage of foreign bodies is slight. Of course, even if the protective mechanism is working satisfactorily a certain amount of finely divided particles, dust, bacteria, etc., may pass the larynx, or food may occasionally enter, but the danger under physiological conditions is minimal compared to that when pathological conditions are met with in nose, pharynx or larynx. This danger is especially great in cases where the glottis is affected, the entrance of foreign bodies being markedly facilitated when the vocal cords are more or less destroyed by ulceration, when the mucous membrane has lost its sensibility entirely or in part, or in paralysis or paresis of the glottic muscles. The dangers are also great in cases of tracheotomy, congenital fistula of the trachea, communications between the trachea and the œsophagus, as seen in epithelioma, between the trachea and a gangrenous focus in the lung or a suppurating tracheal or bronchial lymph gland, or in cases where an aneurism opens into the trachea or a bronchus.

When foreign bodies have reached any portion of the respiratory tract, and when the protective mechanism has proven ineffective to a greater or less extent, there are other mechanisms by which such foreign bodies may be removed. These mechanisms are the action of the cilia and sneezing and

coughing. The cilia with their constant movement outward are continually sweeping away the small foreign bodies, such as dust and bacteria, which have become adherent to the thin layer of mucus which smoothly coats the mucous membrane of the respiratory tract, and in many cases this is all that is necessary for their removal. The mucus and foreign bodies which are swept by this means to the pharynx are either coughed, hawked up or swallowed. On the other hand, if the foreign bodies are of too great mass, or if the functions of the cilia have been diminished or destroyed by inflammation, this mechanism is incapable of protecting the lungs, and the foreign bodies may be expelled by coughing, or may reach the alveoli where they set up inflammatory changes, are dissolved by the body juices or taken up by the phagocytic cells.

The most important means of removing foreign bodies from the respiratory tract are sneezing and coughing, both of which are explosive expiratory impulses set up in the main reflexly, although the latter may also be voluntarily induced. In sneezing, which acts as a cleanser of the upper respiratory tract, a deep inspiration is followed by an expiration so forcible that the closure of the air passages produced by the application of soft palate to the walls of the pharynx is overcome, and the blast is forced violently through the nose, accompanied by a loud and characteristic noise. Sneezing is usually produced reflexly by stimulation of the endings of the sensory fibers of the trigeminus nerve in the mucous membrane of the nose either by pungent or irritating odors, or by irritating foreign bodies, although when the sensibility of these nerve endings is increased, as in a cold in the head, even cold or warm air may inaugurate the sneezing paroxysm. Sneezing may also be set up reflexly from other parts of the body; for instance, some sneeze at looking at the sun or at a very bright light, others when exposed to cold.

The cleansing of the trachea and the larynx, and to a certain extent of the bronchi, although the cilia assist especially in these last regions, is mainly brought about by the act of coughing, when foreign material is to be removed. Coughing consists of a deep inspiration followed by a forcible expiration, at the beginning of which the glottis is closed so that a condition of high pressure is present in the respiratory tract; when the glottis is finally opened the foreign material is forced into the mouth, the nose being shut off by the soft palate, whence it is gotten rid of either by expectoration or by swallowing, the act of coughing like that of sneezing being accompanied by a characteristic sound. Coughing may be inaugurated in a great many ways, but the most important is by stimulation of the sensory fibers of the superior laryngeal nerve in the mucous membrane of the larynx, the especially sensitive portions being, as Nothnagel has shown, the interarytenoid mucous membrane and the region of the bifurcation, although it may be set up reflexly by stimulation of any of the vagus endings of the respiratory tract, as in the mucous membrane of the bronchi, the pleura (although animal experiments vary in their conclusions in this connection) and, according to some, from irritation of the external auditory meatus to which the auricular branch of the vagus is distributed, or of the root of the tongue to which a small twig passes through the superior laryngeal nerve. Coughing may also be set up reflexly from various other portions of the body, as from the stomach, spleen, liver or uterus, when the feet get cold, when the body is exposed. It may be inaugurated spontaneously. In many of these cases such cough is met with only in extremely nervous people, and is probably due to an irradiation of

The act of coughing is by no means an entirely harmless process. In the first place it has a marked effect on the circulation, producing an increase of arterial pressure, due partly to the violent contraction of the expiratory muscles, but more to the effect of the act upon the intrathoracic pressure, there being either a diminished negative pressure, or more commonly a positive pressure; both of these conditions act as impediments to the flow of blood from the systemic veins into the heart, and thus a varicose condition of the facial veins and capillaries results, which may become permanent, while during very acute paroxysms, rupture of the capillaries, as those of the eye or of the brain, is not uncommon. Besides the effect upon the arterial, venous and capillary systems the act of coughing also affects the heart secondarily. In the second place, the act of coughing has a very marked effect on the respiratory organs themselves, for the fact that in coughing a very forcible expiration coincides with closure of the glottis means that until this closure is overcome the lungs are under a considerable degree of tension, which produces an increased pressure in the bronchi and the alveoli. This is mainly in the superior portion of the lung, since in the expiratory contraction of the diaphragm and the other expiratory muscles the lower half of the thorax is most affected, and the air is consequently driven into the upper lobe, producing, if the paroxysms are sufficiently severe or sufficiently frequent, either bronchiectasis or emphysema, or both. Such conditions are peculiarly liable to occur in diseases such as pertussis or bronchial asthma, where the paroxysms are severe and the disease is of considerable duration. Due to the factors mentioned above there is a marked bulging out of certain flexible parts of the thorax during coughing, especially the supraclavicular regions, and the upper intercostal spaces; this is especially well seen in emphysema.

As to the mechanisms of the different kinds of cough, Sahli has paid considerable attention to the matter and mentions numerous types of cough; thus, the moist cough due to the presence of fluid secretions in the bronchi and trachea; the dry cough where no secretion is present or where its consistency is such that the cough is unable to remove it; the raw barking cough with a hoarse or aphonic voice met with in certain forms of laryngitis and due to the swollen condition of the vocal cords, although we may meet with it also in hysteria; the raw, but not barking, cough met with in cases of ulceration or partial destruction of the cords and due to their irregular position; the soundless cough, where the glottic closers have become weakened from ulceration, from paralysis of the glottic closers, from paresis of the expiratory muscles, or general weakness; the hollow or empty cough sometimes met with in severe cases of tuberculosis, due in some cases to diminished strength of the glottic closers and closure of the mouth, in other cases to the aërial resonance in the tuberculous cavities; slight cough due to the irritant being slight, and usually not associated with much secretion and frequently met with in chronic catarrhal conditions of the upper air passages; and violent coughing paroxysms due to intense excitants or irritants, or due to an increased sensibility of the nervous cough apparatus; in such cases, by central irradiation from the coughing centre in the medulla, vomiting may occur, while due to the compression of the intrathoracic veins venous stasis may be so great as to lead to unconsciousness or epileptiform convulsions.

## PATHOLOGICAL CONDITIONS AFFECTING THE NEUROMUSCULAR RESPIRATORY APPARATUS.

In the preceding pages it is assumed that the neuromuscular mechanism which carries out the respiratory movements is normal, but this is frequently not the case. Although there are many variations of the respiratory movements which fall within the normal limits, such as the different modes and rates of breathing met with in children, women and men, during and after exercise or due to emotional influences, nevertheless these are of no especial moment because of the fact, as Voit and Pflüger have shown, that all such alterations have no other influence on the gases of the blood than that involved in the augmented work of the respiratory muscles. For respiration to be normal it is essential that the inspiratory muscles, which overcome the resistance of the ribs, the elasticity of the lungs and the abdominal muscles, must be in a healthy condition, while as regards quiet expiration it is essential that the elasticity of the lungs and thorax should not be impaired: in other words, the regular process of inspiration depends on the ability of the proper muscles to contract properly, while normal expiration requires the occurrence of muscular relaxation at the proper moment, when the elasticity of the lungs and of the ribs if normal effects the rest. There are numerous pathological conditions which may effect the respiratory muscles: thus, the diaphragm may possess congenital or acquired defects which allow the entrance of some of the abdominal contents into the thoracic cavity, while occasionally we may find a complete unilateral rupture of the diaphragm or the absence of one-half or the whole of this muscle.

The functional power of the diaphragm and other respiratory muscles may be impaired by various pathological processes which bring about considerable loss of contractile power, such as severe pyretic diseases, emphysema, chronic bronchitis and heart disease, great debility and progressive muscular atrophy, extensive cancerous infiltration, trichinosis which mainly affects the diaphragm and the intercostals, and contiguous inflammation, such as diaphragmatic pleurisy, peritonitis and pericarditis, which affect the diaphragm partly by the extension of the inflammatory process, partly by the associated circulatory disturbances; various conditions affecting the nervous respiratory apparatus, such as paralysis of certain of the muscles, due either to a central cause, such as medullary hemorrhage, or to a peripheral cause, as in multiple neuritis, lead poisoning, etc., conditions affecting the thoracic cage itself, such as extensive ossification of the costal cartilages, ankylosis as in arthritis deformans, and comparative immobility of the thorax, as seen especially in emphysema, where the thoracic cage tends to assume constantly the shape of forced deep inspiration; conditions where inspiration is associated with pain, such as recent fracture of the ribs, pleurisy, trichinosis, pericarditis, peritonitis and appendicitis; conditions associated with an increase in the resistance to be overcome by the inspiratory muscles, such as large abdominal tumors, much abdominal fat, ascites, meteorism, tympanites, pregnancy and pericarditis with effusion. At times one side of the mechanism is mainly affected, such as unilateral weakness or paralysis of the muscles, unilateral fixation of the thorax, and kypho-scoliosis. As regards expiration, the most important factors are those in which the elasticity of the respiratory apparatus is affected, such as the lessened elasticity of the thoracic wall and thoracic muscles, lessened elasticity of the

lung tissue, met with especially in emphysema, and tonic contraction of the diaphragm; while as regards the muscles which come into play in forced expiration, they may be affected by any of the pathological conditions mentioned as affecting the inspiratory muscles.

The immediate effect of the impediments to inspiration and expiration, as regards the gaseous contents of the blood, is that not enough oxygen enters the lungs, due mainly to the former, and not enough carbon dioxide leaves the lungs due mainly to the latter; so that conditions arise which soon make life impossible if respiration is not modified so as to correct them. There are two means of accomplishing this; first, the reduction of oxygen consumption, which may be brought about by lessening as far as possible the amount of muscular work, and by living a life as quiet as possible, and second, by increasing either the depth or the frequency of the respiratory movements. In the main these conditions act mechanically very much like a stenosis of the air passages, and may be similarly corrected, that is, if the impediment affects inspiration, the inspiratory movements become stronger, and frequently also slower, while if the expiratory portion of the apparatus is at fault active takes the place of passive expiration, and here the abdominal muscles play the most important role. If certain groups of muscles alone are affected, compensation may be brought about by the transference of work to the more capable muscles; thus, thoracic may be converted into abdominal breathing, and *vice versa*, while in conditions where one side alone is affected compensation may be brought about by an increase of movement of the normal side; in those rare cases where the diaphragm is absent, not only must the work be done by the other inspiratory muscles, but the pressure relations must be properly maintained by the abdominal muscles. On the other hand, in a number of cases deeper respiratory movements either are ineffective or impossible, and in such conditions regulation is brought about by more rapid, shallower respirations; such regulation is met with when deep breathing is productive of pain, in cases where practically all the respiratory muscles are affected by the pathological process, and in cases where there is an increased resistance to inspiration, such as emphysema and the various abdominal conditions mentioned. In many of these conditions an attempt is often made first to regulate respiration by the method previously described, that is, deeper inspiration; but either the resistance cannot be overcome by this means, or the muscles are not sufficiently strong to keep up such a mode of compensation. In the case of shallow respirations there is an especially marked tendency for atelectasis, bronchial catarrh and even pneumonia to develop because of the imperfect ventilation of certain parts of the lungs, notably the deeper portions.

The utility of regulating the respiratory mechanism so that more oxygen enters and more carbon dioxide leaves the lungs, and of regulating the oxygen demand by modifying the mode of life is easily apparent, for in those conditions the active manifestations of which pass off after a greater or less period of time, such as meteorism, typhoid fever, trichinosis, etc., life is sustained until the normal conditions have been restored, while even in those cases where complete recovery is impossible, life may not only be rendered possible for a number of years, but may even be rendered supportable.

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The functional power of the diaphragm and other respiratory muscles may be impaired by various pathological processes which bring about considerable loss of contractile power, such as severe pyrexial diseases, emphysema, chronic bronchitis and heart disease, great debility and progressive muscular atrophy, extensive cancerous infiltration, trichinosis (which mainly affects the diaphragm and the intercostals), and contiguous inflammation, such as diaphragmatic pleurisy, peritonitis and pericarditis, which affect the diaphragm partly by the extension of the inflammatory process, partly by the associated circulatory disturbances; various conditions affecting the nervous respiratory apparatus, such as paralysis of certain of the muscles, due either to a central cause, such as medullary hemorrhage, or to a peripheral cause, as in multiple neuritis, lead poisoning, etc., conditions affecting the thoracic cage itself, such as extensive ossification of the costal cartilages, ankylosis as in arthritis deformans, and comparative immobility of the thorax, as seen especially in emphysema, where the thoracic cage tends to assume constantly the shape of forced deep inspiration; conditions where inspiration is associated with pain, such as recent fracture of the ribs, pleurisy, trichinosis, pericarditis, peritonitis and appendicitis; conditions associated with an increase in the resistance to be overcome by the inspiratory muscles, such as large abdominal tumors, much abdominal fat, ascites, meteorism, tympanites, pregnancy and pericarditis with effusion. At times one side of the mechanism is mainly affected, such as unilateral weakness or paralysis of the muscles, unilateral fixation of the thorax, and kypho-scoliosis. As regards expiration, the most important factors are those in which the elasticity of the respiratory apparatus is affected, such as the lessened elasticity of the thoracic wall and thoracic muscles, lessened elasticity of the

lung tissue, met with especially in emphysema, and tonic contraction of the diaphragm; while as regards the muscles which come into play in forced expiration, they may be affected by any of the pathological conditions mentioned as affecting the inspiratory muscles.

The immediate effect of the impediments to inspiration and expiration, as regards the gaseous contents of the blood, is that not enough oxygen enters the lungs, due mainly to the former, and not enough carbon dioxide leaves the lungs due mainly to the latter; so that conditions arise which soon make life impossible if respiration is not modified so as to correct them. There are two means of accomplishing this; first, the reduction of oxygen consumption, which may be brought about by lessening as far as possible the amount of muscular work, and by living a life as quiet as possible, and second, by increasing either the depth or the frequency of the respiratory movements. In the main these conditions act mechanically very much like a stenosis of the air passages, and may be similarly corrected, that is, if the impediment affects inspiration, the inspiratory movements become stronger, and frequently also slower, while if the expiratory portion of the apparatus is at fault active takes the place of passive expiration, and here the abdominal muscles play the most important role. If certain groups of muscles alone are affected, compensation may be brought about by the transference of work to the more capable muscles; thus, thoracic may be converted into abdominal breathing, and *vice versa*, while in conditions where one side alone is affected compensation may be brought about by an increase of movement of the normal side; in those rare cases where the diaphragm is absent, not only must the work be done by the other inspiratory muscles, but the pressure relations must be properly maintained by the abdominal muscles. On the other hand, in a number of cases deeper respiratory movements either are ineffective or impossible, and in such conditions regulation is brought about by more rapid, shallower respirations; such regulation is met with when deep breathing is productive of pain, in cases where practically all the respiratory muscles are affected by the pathological process, and in cases where there is an increased resistance to inspiration, such as emphysema and the various abdominal conditions mentioned. In many of these conditions an attempt is often made first to regulate respiration by the method previously described, that is, deeper inspiration; but either the resistance cannot be overcome by this means, or the muscles are not sufficiently strong to keep up such a mode of compensation. In the case of shallow respirations there is an especially marked tendency for atelectasis, bronchial catarrh and even pneumonia to develop because of the imperfect ventilation of certain parts of the lungs, notably the deeper portions.

The utility of regulating the respiratory mechanism so that more oxygen enters and more carbon dioxide leaves the lungs, and of regulating the oxygen demand by modifying the mode of life is easily apparent, for in those conditions the active manifestations of which pass off after a greater or less period of time, such as meteorism, typhoid fever, trichinosis, etc., life is sustained until the normal conditions have been restored, while even in those cases where complete recovery is impossible, life may not only be rendered possible for a number of years, but may even be rendered supportable.

## ABNORMAL CONDITIONS OF THE PULMONARY CIRCULATION, OF THE BLOOD AND OF THE RESPIRED AIR.

It is essential that the pulmonary circulation be unimpeded for the proper oxygenation of the blood. Because of the slight degree of resistance in the pulmonary circulation the blood flows through the lungs under a low tension, but with considerable velocity, which velocity is increased with each inspiration, diminished with each expiration. In a number of conditions sections of the vascular system of the lungs have been rendered impervious, as for example by thrombi or emboli in the branches of the pulmonary artery, various cirrhotic processes of the lung, tuberculous or bronchiectatic cavities, caseation of the lung, pulmomary emphysema, where many capillaries have been destroyed with the alveolar septa, compression of the lungs by intra-thoracic and intra-abdominal tumors, by pleuritic effusions, in certain cases of pneumothorax, and by pericarditis with effusion. In the second place, the pulmonary circulation may be affected even when the vessels of the lungs are pervious and undiminished in number, as in various cardiac lesions, where either the force of the right ventricle is diminished or the resistance to the flow of blood into the left ventricle is increased, fatty degeneration of the heart, lesions of the pulmonary orifice, extreme pericardial effusion, complete adherence of the two layers of the pleura, and atelectasis and chronic bronchitis, where in the affected portions it may be difficult or impossible for the lungs to dilate during inspiration. Under any of these conditions, whether the blood channel be diminished or the blood stream slowed, less blood passes through the lungs, and some form of compensation is therefore necessary. This is mainly brought about by the circulatory apparatus itself, although in certain cases it is not perfect, as when the heart muscle is seriously affected, and when the derangement of circulation is absolutely too great; in such cases attempted regulation by means of a modification of the respiration is more apparent. In all cases, but especially in this latter class, there is a diminution of oxygen and an increase of carbon dioxide, and, due to the effect of the altered blood upon the respiratory centre, the respirations become deeper, which raises the partial pressure of the oxygen in the alveoli as well as quickens the circulation; the rate of respiration is sometimes slowed, sometimes quickened. As to the utility of these dyspnœic respiratory movements, according to some observers, Filehne for instance, the form of dyspnœa in patients suffering with heart disease is absolutely useless, but this is not so, for these dyspnœic movements further the pulmonary circulation as well as increase the partial oxygen pressure.

In anæmia we again have a condition in which unless some form of compensation occurs proper oxygenation is impossible, and this is so whether the condition be one of oligocythæmia or oligochromæmia. In such conditions the effect of the increase in the carbon dioxide and decrease in the oxygen of the blood upon the respiratory centre is to bring about a dyspnœic respiration (there being both a strengthening and a quickening of the respiratory movements). This mechanism tends to regulate the condition, for the exchange must be more rapid because the pulse is quicker, and the partial pressure of the oxygen in the alveoli must be increased as well. By such a mechanism the total gaseous exchange may be normal, but internal respiration is always affected. In other conditions in which the blood is

abnormal, respiration is modified, as for example in cholera where there is marked retardation of the circulation; in uræmia (where the slowing of the respiration with special prolongation of the expiratory phase is probably referable to the effects of the circulating toxins upon the respiratory centre, although many of the respiratory symptoms met with in this condition are referable to the associated myocarditis, bronchitis, or pulmonary œdema) and diabetes, where the deep breathing frequently met with is possibly due to a lessened oxygen capacity of the blood, possibly to the effect of the abnormal blood upon the respiratory centre.

The characteristic effect of hyperpyrexia upon the respiration is an increased frequency, the so-called heat tachypnœa, and it has been shown by experiments upon animals that this is due to the stimulation of the respiratory centre by the blood warmer than normal. Of course, the toxins which are frequently present have some effect.

The variation in composition of the respired air also plays a most important part, as the penetration of gases through the epithelial cells of the lung is mainly dependent on the partial pressure of the alveolar air. The effect of diminution of air pressure is well known, the degree of intensity of the symptoms depending upon the extent of the diminution and upon the special susceptibility of the individual and the condition of his respiratory, circulatory, and hæmatopoietic systems. Dyspnœa, headache, great fatigue, drowsiness, and sometimes even complete unconsciousness are met with in those ascending great heights, and although these symptoms are partly due to the effect of the cold, wind, muscular exertion, and the lower barometric pressure, they are in the main referable to the diminution of the partial pressure of the oxygen in the alveoli. It is well recognized, however, that the majority of men are capable of enduring a diminution of air pressure to 450 or 400 mm. of Hg. without discomfort, and in some cases even one-half an atmosphere. As regards the effect of the diminution of air pressure on the exchange of gases, Fränkel, Geppert and Loewy have shown that there is no change in the gaseous exchange if the pressure is one-half an atmosphere or more, while if it is less than this there is an increase in the carbon dioxide production, and also a slight increase in the oxygen intake, due to the increase of the respiratory movements. The regulating power of the respiratory mechanism is exceedingly striking; thus, at a partial oxygen pressure of 72 mm. Hg. the hæmoglobin saturation is 96.7 per cent., while at 99 mm. Hg. it is 97.6 per cent., according to Hüfner; according to Loewy, at a barometric pressure of 356.5 mm. Hg., the hæmoglobin saturation is 92 per cent. As to the regulatory mechanism in these cases, a superficial, more rapid type is usually met with, due partly to the ascent of the diaphragm produced by the expansion of the intestinal gases, while if the pressure sinks still further, deeper respirations make their appearance. According to Fränkel and Geppert, the oxygen content of the blood is not appreciably changed with a pressure of 410 mm. Hg., although Loewy has shown that the high climate affects the regulatory mechanism apart from the lowered oxygen tension, possibly due to its effect on the circulation and on the hæmoglobin. As to increased density of the air, Loewy has shown that even twice an atmosphere has no appreciable influence upon the respiratory mechanism.

As regards the effect of carbon monoxide on the respiratory mechanism, if it is present in the air to a greater extent than 0.8 to 1 per 1,000, carbon-

monoxide hæmoglobin is formed, which affects the organism partly by lessening the amount of oxyhæmoglobin, partly by the effect of the carbon monoxide upon the nerve endings. The mechanical effects of carbon monoxide poisoning are exactly the same as those produced by slow bleeding or by gradual diminution of the respiratory surface.

The effect of all the preceding conditions depends upon a number of factors besides the degree or extent of the pathological condition presented, such as the age, the functional condition of the respiratory bones and muscles, the physical condition of the organs and tissues of the body and the ability of the patient to rest and avoid strain.

## CERTAIN ADDITIONAL QUESTIONS IN THE MECHANICS OF THE RESPIRATORY DISEASES.

**Dyspnœa.**—It must be remembered that dyspnœa is essentially a form of regulation designed to counteract the existing impediment or pathological condition, while the extent of the dyspnœa depends upon the degree of oxygen deficiency. Of course, by rest and regulation of the mode of life it is possible to diminish the consumption of oxygen, but this and the elimination of carbon dioxide cannot be reduced below a certain minimal amount, while it is a practical impossibility to spare for any considerable length of time all muscles except those absolutely necessary. The term dyspnœa is used in a double sense, first to signify increase in the rate or in the depth of the respirations, or labored and slow respirations (in other words, objective dyspnœa), and second, the sensation of air hunger (subjective dyspnœa). Due to the regulatory mechanism the patient may have the former without the latter, while in certain conditions, notably hysteria and melancholia, we may have the latter without the former. We must carefully differentiate objective and subjective dyspnœa, realizing that the former may not necessarily always produce the latter. In some cases subjective dyspnœa is not present, as in many patients at rest suffering from kyphosis, chronic bronchial catarrh, extensive pleural adhesions, moderate emphysema, and small tuberculous foci, although in all these conditions objective dyspnœa is present.

Subjective dyspnœa is almost always present in extreme grades of emphysema, advanced tuberculous lesions, extensive acute pneumonia, stenosis of the trachea, and pneumothorax. Although persons with impaired respiration instinctively limit the expenditure of oxygen, and although in slighter impediments to respirations, even though the oxygen saturation of the blood is below normal, a certain equilibrium is established in the organs and tissues, nevertheless, if conditions supervene which demand a larger amount of oxygen, such as exertion or fever, or in which the equilibrium between the blood and the organs is not maintained, we meet with definite signs of the imperfection of the respiratory mechanism, partly in the form of subjective dyspnœa and partly in the form of cyanosis. As Sahli says, the presence of marked objective dyspnœa without cyanosis is a clinical proof of the view that the intensity of the respiratory movements is not entirely dependent upon the grade of the aëration of the blood, but is influenced directly by hindrances to respiration. Thus, under all conditions objective dyspnœa seems to diminish cyanosis and the feeling of subjective dyspnœa, but in all

severe hindrances to respiration, especially where the neuromuscular respiratory mechanism is not normal, cyanosis will be present sometimes to a considerable degree, although even in these conditions the organism may finally accommodate itself to the impoverished blood, and the organs may perform their functions comparatively well, and with this there is, as a rule, less and less subjective dyspnœa. There are also true compensatory changes on the part of the organism itself, notably in the circulatory apparatus, which aid in this regulation, because the overloading of the blood with carbon dioxide stimulates the vasomotor centre, and also frequently the vagus itself, tending to slow the heart beat and thus diminish the demand for oxygen.

**Changes in the Respiratory Centre; Cheyne-Stokes Breathing.**—That the regulatory mechanism of respiration should be carried on satisfactorily it is essential that the respiratory centre itself should be normal, but there are a number of conditions in which this centre is pathologically affected, as shown by abnormal forms of respiration. Of these none is more interesting than the so-called Cheyne-Stokes respiration, a periodic form met with in a large number of conditions and generally of grave prognosis. Among the conditions in which it is seen, are various severe affections of the brain, such as tumors and hemorrhage; various cardiovascular affections, such as fatty heart, coronary sclerosis, non-compensated aortic stenosis, arteriosclerosis; various diseases of the respiratory apparatus, especially those associated with unconsciousness, and chronic nephritis. It has also been noted in healthy children, or even adults, especially during sleep, while Filehne has shown that it may be produced experimentally in rabbits by the hypodermic injection of morphia, and it is a well-known fact that the administration of morphia increases the tendency to this type of breathing in those so predisposed. Associated with this peculiar form of respiration, characterized by inspirations of gradually increasing depth, reaching a maximum and then diminishing and followed by a pause, sometimes lasting as much as forty-five seconds, are other associated phenomena; thus, during the respiratory pause there is often a marked slowing of the pulse, a distinct narrowing of the pupils, while marked symptoms of air-hunger are often met with during the phase of increasing inspiratory efforts.

There are various explanations of this condition, although all agree that it has much to do with the reduction of irritability of the respiratory centre due to long-continued impairment of the arterial circulation in the medulla. The original theory of Traube was that it was due primarily to the diminution of the excitability of the respiratory centre, because of the lack of the proper amount of oxygen, and, due to this, the physiological stimulants during the pause are not sufficient to set up respiratory movements; the blood thus becomes more strongly venous and, this forming a more intense stimulation for the respiratory centre, respiration begins and continues until the blood reaches a certain degree of richness in oxygen and poverty in carbon dioxide which is an insufficient stimulus to the centre, and then the pause recurs. Sahli explains certain discrepancies in this theory by calling attention to the fact that the blood becomes more venous even after the beginning of respiration, which accounts for the gradual increase in strength of the respiratory movements, and in the second place, that the excitability of the centre is inherent and not altogether dependent on the circulation. Rosenbach believes that the periodicity of respiration depends upon an abnormal con-

dition of fatigue of the respiratory centre, while Unverricht holds that it is due to a disturbance in the connection between the respiratory centre in the medulla and certain portions of the cortex. Filehne thinks that the main cause is an excitation of the vasomotor centre causing primarily a contraction of the brain capillaries, and secondarily an affection of the respiratory centre due to the anæmia; in other words, that the respiratory centre is affected by the anæmia, which in turn is produced by stimulation of the vasomotor centre.

That form known as Biot's respiration, which is especially frequent in meningitis but is also seen in other brain diseases and severe general diseases, characterized by respiratory pauses lasting from several seconds to one-half a minute or more, repeated more or less periodically, is also unquestionably due to changes in the respiratory centre. The extremely deep respirations met with in various poisonings and intoxications, as uræmia, diabetes, hydrocyanic acid poisoning, and typhus fever, are in all probability due to the effect of the poison upon the respiratory centre.

Recently, Eyster has been studying Cheyne-Stokes breathing by means of the Erlanger sphygmomanometer. He found two groups of cases, first, those with a rise of blood pressure and an increase of pulse rate during the period of dyspnœa, with a fall during the period of apnœa, and second, those with a fall during dyspnœa and a rise during apnœa. In the latter class were the cases associated with cardiac and arterial disease, while of the former class Eyster had two cases, one of cerebral hemorrhage, the other with a history of intense headache and left-sided clonic spasm with a choked disk in the left eye. Eyster found that in the first group, that is, cases associated with increased intracranial tension, the underlying condition of periodic respiration is an alternate anæmia and period of blood supply of the brain and medulla, the former being associated with apnœa, and occurring when the blood pressure is below the line of intracranial pressure, while the period of respiratory activity is associated with the period of blood supply to the brain, and occurs with the rise of the blood pressure above that of the intracranial pressure. The reason that these changes in blood supply should cause the opposite effect upon the respiratory centre to those observed is that the irritability of this centre is periodically much reduced or even lost when the blood pressure is below the line of intracranial pressure. Eyster was unable to give a satisfactory explanation in the second group of cases.

**Mode of Death in Respiratory Diseases; Asphyxia and Slow Suffocation.**—While in many cases the dyspnœic respiration is the means of saving life, and while in all cases life is prolonged thereby, nevertheless there are many conditions in which the external respiratory disturbances are greater than can be compensated by the modified respiratory movements, and thus suffocation occurs, the clinical picture being markedly different according to whether the condition is suddenly or gradually produced. In human pathology we do not often meet with cases of death by acute asphyxia; it is seen, however, in certain conditions, such as complete and sudden occlusion of the pulmonary artery, fatal spasm of the glottis, constriction of the trachea, large hemorrhage filling up all the bronchi, sudden paralysis of the respiratory muscles, sudden bending of the trachea in patients with goitre, and those rare cases of unilateral pneumothorax suddenly complicated by pneumothorax of the other side. On the other hand, slow suffocation is the cause of death in a large number of respiratory conditions, as in

glottic or pulmonary œdema, laryngeal diphtheria, pneumonia, bronchitis, pleural effusion, trichinosis, emphysema and pulmonary tuberculosis, in which for days, weeks or months the respiratory disturbances have been present. The mechanical conditions which may lead to slow suffocation are many; the impediments to respiration may gradually increase, finally reaching such a point that the strongest dyspnœic respiration is incapable of correcting the condition.

The picture in acute asphyxia or sudden suffocation is an extremely striking one, characterized by the most violent, stormy and deep respirations, with dilated nostrils, wide open mouth, stretched out neck, the head back, and all the accessory respiratory muscles as well as many other muscles actively involved. The vasomotor centre is strongly excited, and we have a contraction of the sphlanchnic vessels, a dilatation of the cutaneous vessels, and an increase in the arterial pressure, while the heart is slowed from the strong vagus stimulation, all of these factors helping to bring the maximum amount of blood to the brain. The patient shows marked restlessness, and then convulsions of gradually increasing intensity, leading to a condition of complete insensibility or paralysis, with a few feeble respiratory efforts separated by long pauses, and finally death, with a diminution of the arterial tension during the final stage, and a tendency of the cardiac contractions to persist after respiration has ceased As to the explanation of acute asphyxia, there is some difference of opinion as to whether the sudden stoppage of oxygen or the marked increase of carbon dioxide plays the larger role, but the experiments of Rosenthal and others seem to show that the former is the more important factor.

Slow suffocation is not a striking picture, and is not marked by the stormy phenomena so characteristic of acute asphyxia. There is usually a complete absence of the strikingly irritative phenomena, there is no marked increase of dyspnœa, no convulsion, and no evidence of irritation of the vasomotor and vagus centres. The pulse is usually small, the body movements feeble and languid, the temperature often low, the skin cool The picture is one of a gradual narcosis of the various centres, and all the functions become less and less active. There is no especial complaint of air-hunger, nor is the picture one of striking objective dyspnœa, the accessory muscles being often not used at all; the respirations become frequent and shallow, gradually becoming weaker until life fades away. In this condition we sometimes meet with Cheyne-Stokes breathing and other modifications of respiration due to the changes in the respiratory centre. As to the cause of the phenomena of slow suffocation, here also it is still a question of dispute whether the impoverishment of the blood in oxygen, or the accumulation in it of carbon dioxide plays the more important role

In certain conditions we have a state half-way between that of acute asphyxia and slow suffocation, and the picture presented bears a resemblance to each of the two; thus, the irritative phenomena of acute asphyxia are seen to a certain extent but the narcotic phenomena of slow suffocation modify their manifestations.

# CHAPTER XV.

## DISEASES OF THE NASOPHARYNX, PHARYNX AND TONSILS.

By FRANCIS R. PACKARD, M. D.

### ACUTE NASOPHARYNGITIS.

**Etiology.**—Acute inflammations limited strictly to the nasopharyngeal region are of rather rare occurrence. When they do occur they are usually exacerbations of a chronic inflammatory condition of the nasopharynx. The mucous membrane of the nasopharynx being continuous with that lining the nose is almost always more or less involved in inflammations of the Schneiderian membrane, and frequently after the rhinitis has disappeared the nasopharyngitis which has been associated with it remains. Occurring primarily, acute nasopharyngitis is generally the result of exposure to cold or damp. It is very apt to follow sudden changes in temperature. It is occasionally seen in connection with digestive disturbances. It sometimes arises from the inhalation of irritant vapors or dust. It is apt to occur in conjunction with or following upon acute infectious diseases such as scarlet fever and diphtheria.

**Pathology.**—The manifestations are those of acute catarrhal inflammation of the mucous membrane. There is the usual stage of acute engorgement of the bloodvessels, followed by increased glandular activity with profuse secretion The inflammation either subsides by the ordinary processes of resolution, or may assume a chronic form.

**Symptoms.**—The patient's first complaint is generally of a sensation of discomfort in the back of the throat. At first there is a dry cough. After some days the secretion, which is at first clear and white, becomes thick and muco-purulent and may be quite profuse. The attack is apt to be attended with slight fever, the temperature rising to 101° F. Occasionally the patient will complain of tinnitus and a sensation of fulness in the ears owing to occlusion of the pharyngeal extremities of the Eustachian tubes.

**Treatment.**—Nothing affords more comfort than douching the nasopharyngeal space with warm normal salt solution, or with a warm alkaline antiseptic solution This may be accomplished either by allowing the patient to snuff up the solution through the nares, or by the physician injecting the solution into the nasopharynx by means of a postnasal syringe. Should the patient complain of much sore throat and pain, it is comforting for him to inhale hot medicated vapors. For this purpose there is nothing more satisfactory than the compound tincture of benzoin inhaled in hot water After cleansing the nasopharynx, great lessening of the congestion will be produced if a strong solution of nitrate of silver be applied on a cotton pledget directly to the mucous membrane. The nasal passages should be kept open in order that respiration may be free, and for this the local application of adrenalin solution (1 to 5,000) is useful. This should be followed by the use of a bland oil spray containing a little camphor and menthol.

## CHRONIC NASOPHARYNGITIS. (POSTNASAL CATARRH.)

**Etiology.**—Chronic nasopharyngitis may be the result of repeated attacks of acute nasopharyngitis. More usually, however, frequent acute attacks of nasopharyngitis are the manifestations of an underlying chronic inflammatory condition. Chronic nasopharyngitis is frequently one of the manifestations of the gouty or rheumatic diathesis, and is very commonly associated with gastro-intestinal disturbances It is a frequent sequel of acute infectious diseases, especially influenza, scarlet fever, and diphtheria. The abuse of alcohol is a very common cause, chiefly because of the digestive disturbances which are engendered by it. Chronic nasopharyngitis frequently results from, or, if it exists, is kept up by the use of tobacco. Intranasal deformities, or chronic obstructive conditions within the nose, often cause the pharyngeal mucous membrane to become inflamed, and the condition continues until the cause is removed. Of the direct causes of chronic nasopharyngitis, the most common is exposure to a damp climate in which the patient is subjected to sudden variations of temperature. Thus it is especially prevalent near the Atlantic seaboard of the eastern United States. Occupation is frequently not only a predisposing but also an exciting cause when it exposes the patient to the inhalation of irritant vapors or dust.

**Symptoms.**—The most characteristic symptom of a chronic nasopharyngitis is the sense of irritation which is almost constantly present in the nasopharynx, causing the patient to have a tendency to hawk, in an effort at relief. This only serves to irritate the inflamed structures yet further. Frequently the patient's throat becomes so sensitive and the irritation so great, that retching or even vomiting results The patient complains of continuous postnasal dropping of mucus. There is, as a rule, not very much secretion to expectorate, such as there is being thick, tenacious, and slimy. In advanced cases the discharge is apt to be muco-purulent and greenish, and occasionally we see the formation of crusts and scales, which are apt to be somewhat blood-stained because of abrasion of the mucous membrane. The secretion in the postnasal space frequently undergoes decomposition and renders the breath most offensive. The voice is generally husky and without the proper resonance. There are very apt to be aural disturbances, sometimes of quite marked severity, because of obstruction of the pharyngeal orifice of the Eustachian tube, occasionally from the extension of the inflammation up the tube, and at times because of the nasopharyngeal secretion entering the tube The mucous membrane of the pharynx or larynx may show catarrhal changes. Disturbances of digestion are very common with chronic nasopharyngitis, generally taking the form of dyspepsia. On examination the nasopharynx will be seen to contain a quantity of thick stringy secretion, upon the removal of which the mucous membrane will present a dry, glazed and congested appearance. Sometimes there is considerable swelling, so that it is hard to inspect the upper portions of the postnasal space.

**Treatment.**—Of all the measures, none are more efficacious than those which deal with general hygiene. The clothing should be regulated in order that the patient's bodily temperature may be kept as even as possible. For this purpose he should wear, both winter and summer, some form of mesh underwear. Undergarments of this character permit free evaporation of the

perspiration and do more to further the activity of the skin and to prevent chilling of the surface than anything else. Thick flannel undergarments should be particularly avoided, as they induce perspiration and prevent evaporation. If the patient is able to stand a cold tub bath every morning it will greatly promote the circulatory activity of the skin. If he cannot take the plunge or shower bath, he may at any rate douche his neck, shoulders and chest with cold water. Careful instruction should be given as to the proper ventilation of his bedroom, as these patients are very apt to form an idea that "taking cold" is promoted by night air, and hence they exclude it. If the patient leads too sedentary a life, some regular form of exercise should be prescribed and insisted upon. Dietetic errors should be sought for and corrected, and the use of tobacco and alcohol regulated, or, if necessary, interdicted.

The patient should be given an alkaline antiseptic douche with directions to snuff it up through the nostrils into the nasopharynx, following which he should be directed to use a bland oil spray. Locally there are many substances which prove of value, their usefulness varying greatly in different cases. At least two or three times a week, at the commencement of treatment, the physician should himself thoroughly cleanse the nasopharynx, and apply some astringent or alterative preparation to the inflamed mucous membrane according to the indications present. For thorough cleansing it will generally be found necessary not only to use a solution through the anterior nares, but also to wash out the nasopharynx with some form of postnasal syringe. Any of the ordinary alkaline antiseptic solutions may be used, such as Dobell's solution, or those which are made up as the various so-called antiseptic nasal tablets. Should the secretion in the nasopharynx be very offensive, a weak potassium permanganate solution used as a douche will often give the most gratifying results. After the muco-pus which has collected in the postnasal space has been removed, nitrate of silver in a solution of 30 or 60 grains to the ounce may be applied with cotton on an applicator, and will prove more generally useful than any other application. In mild cases, glycerole of tannin will frequently prove of value. Should there be a very granular condition of the mucous membrane, it is well to try the application of some caustic, such as lactic acid in a strength of 1 dram to the ounce. If the physician uses a strong caustic, great care should be taken that the neighboring healthy tissues are not touched. For this purpose the application should be made only with a good reflected light. If there is a quantity of granulation tissue requiring thorough extirpation, its destruction by means of the electric cautery is sometimes necessary. This is a very delicate procedure and should only be performed by one who is accustomed to the performance of delicate manipulations within the throat. If the cautery is misapplied the cicatricial contractions which follow may be of the most serious character.

## HYPERTROPHY OF THE LYMPHOID TISSUES IN THE NASOPHARYNX. ADENOID GROWTHS IN THE NASOPHARYNX. HYPERTROPHY OF THE PHARYNGEAL TONSIL.

This condition is really an hypertrophy of the glandular tissue which normally exists to a greater or lesser extent in the vault of the pharynx, in other words, of the tissue which is generally known as the "pharyngeal

tonsil." The term "third tonsil" is frequently applied to these adenoid vegetations. The condition was first thoroughly studied and described by Wilhelm Meyer, a Danish surgeon, and since his time has been generally recognized as the most frequent cause for mouth breathing in children. Its etiology is obscure. It undoubtedly occurs most commonly in conjunction with enlargement of the faucial tonsils, and is accordingly spoken of as one of the manifestations of the lymphatic diathesis, in which there is widespread hypertrophy of all lymphoid structures. Although it occurs with marked frequency in children who suffer from tuberculous or syphilitic taint, it is, nevertheless, seen in the children of healthy parents, and it would seem more rational to consider its presence in children who had inherited tuberculosis or syphilis, as a result of the anæmia attendant upon those conditions rather than as a manifestation of the inherited disease.

Climatic conditions undoubtedly exercise an influence in the causation of enlargement of the pharyngeal tonsil; thus the condition is much more frequent in low, damp localities in which there are frequent changes of temperature than it is in better climates. Hypertrophy of the pharyngeal tonsil occurs so frequently in certain families that there is no doubt that a hereditary factor is present in many of the cases. It is doubtful if the condition is ever congenital, although a condition of nasal catarrh is often noticeable in young infants in whom there is a subsequent development of adenoid vegetations in the nasopharynx. Kyle holds that the cause of the so-called inherited tendency to adenoids is frequently found in the inherited family nose, the hypertrophy of the glands in the nasopharynx being more common in children whose nostrils have a narrow slit-like orifice than in those whose nostrils are wide open. In both children and adults this glandular hypertrophy is frequently found in association with hypertrophic rhinitis.

**Pathology.**—Adenoid vegetations in the nasopharynx are generally composed of a mass of hypertrophied lymphoid glandular tissue, covered with epithelium. Further down in the structure, there are ramifying trabeculæ of connective tissue with lymphoid cells lying between them. The proportion of lymphoid to connective tissue varies greatly in different specimens, thus, in very young children who have not been subject to repeated inflammatory attacks or congestions of the tissue, the structure is soft and the glandular lymphoid element predominates. In older patients the vegetations have usually been the site of various local congestive and inflammatory changes which have resulted in the deposit of inflammatory material with overgrowth of connective tissue and consequent hardening of the structure. The surface of these growths is generally very markedly lobulated or mammillated. The enlargement of the glands in the nasopharynx is frequently accompanied by hypertrophy of the glandular structures which pass down from the nasopharynx on the sides of the pharyngeal wall. These glands have the same structure as those higher up in the nasopharynx, their enlargement is a part of the same process, and they generally disappear after the removal of the latter.

**Symptoms.**—The most prominent symptoms are those which arise from nasal obstruction, and of these the most striking is the appearance of the face which results from habitual mouth breathing. Everyone is familiar with the aspect of the unfortunate beings who are unable to respire properly through the nose. The dull, expressionless face, lack-lustre eyes, wide-open mouth,

with protruding upper lip and hanging lower jaw, accompanied with an inability to fix the mind upon a task, and the general stupidity and mental dulness frequently lead to their being regarded as mentally deficient. In fact, it is this mental sluggishness to which Guye, of Amsterdam, gave the term "aprosexia" There is also often an associated deficiency of hearing, the result of obstruction of the pharyngeal orifices of the Eustachian tubes. This deafness adds materially to the child's apparent stupidity. These children are rendered more unattractive by the fact that they are generally irritable and cross because of their constant physical discomfort.

The obstruction to nasal respiration is almost invariably most marked at night when the circulation is more sluggish, and mucus more apt to accumulate. This results in restless and disturbed sleep, and frequently in nightmares whereby the child is deprived of natural refreshing slumber, and the discomfort is materially aggravated. Quite often the patient is brought to the physician because of restlessness at night, and for the snoring and grunting which is so noticeable at that time. As a result of the air not being moistened and warmed by its passage through the nasal chambers, patients who suffer from adenoids are also frequently subject to inflammations of the pharynx and larynx, or even to attacks of bronchitis. In this way adenoids are probably the most common exciting cause of asthma and spasmodic croup in young children. The child's voice is affected at a very early stage and in a very characteristic manner. The loss of nasal resonance causes the voice to lose its natural resonance. There is generally considerable mucous discharge from the nose, and a lack of ability to properly expel this causes the child to keep up a continuous sniffling.

Of all the evil results which adenoids may produce, there are none more serious than those which occur in the ear. The aural complications vary greatly as regards their manifestations and their seriousness. There may be attacks of pain due to interference with the patency of the Eustachian tube on the affected side. This same obstruction, however, frequently leads to serious results in the middle ear, the result of constant interference with its proper ventilation through the Eustachian tube, giving rise to chronic catarrhal otitis media, and thus leading to serious impairment of the hearing. More serious, however, is the constant liability to infection of the middle ear with microörganisms which have found their lodgment in the adenoid mass. These vegetations are always found microscopically to be swarming with microörganisms, and there is no doubt that their proximity to the Eustachian tube frequently permits of their access to the middle ear, where they may set up a purulent inflammation and cause the most serious consequences

Children with adenoids are often subjected to repeated attacks of inflammation of the fauces, pharynx and faucial tonsils, particularly when the latter are hypertrophied. As a result of these, there is apt to be enlargement of the lymph glands about the lower jaws and cervical region. The presence of adenoid growths in the nasopharynx is also frequently responsible for the maintenance of a chronic catarrhal conjunctivitis. Peculiarities in the formation of the hard palate, and various irregularities of the teeth are also in many instances to be attributed to the interference with nasal respiration. It is very difficult in many cases to estimate just how far adenoids influence such conditions, but they are no doubt in many instances a considerable factor

**Diagnosis.**—The diagnosis of adenoids generally gives but little difficulty. The peculiar facial expression and the history suffices in many instances to make the condition plain. Examination by posterior rhinoscopy is frequently a difficult matter in children, but enough can usually be seen with a mirror to justify the diagnosis, if the vegetations are present. Examination through the nares with a speculum and probe is sometimes more easily accomplished, and is of great value should it be impossible to make a satisfactory postnasal examination. A digital examination is usually possible, although, as it is terrifying and sometimes painful, it is to be avoided unless deemed absolutely necessary.

**Treatment.**—This consists solely in the removal of the adenoid mass, the only questions being as to the suitable time, the method to be used, and the anæsthetic to be employed. Although their presence in sufficient amount to produce serious symptoms always demands their removal, nevertheless, the demand is not so urgent as to interfere with the surgeon delaying the operation until the patient shall be in the best condition for it. If, as is usually the case, the patient is a child, the general health is apt to be considerably below par, and it is well to give a little time to building up before the operation is performed. It should not be done while there is any acute inflammatory condition in the air passages or ears, as the existing condition will almost invariably be aggravated under such circumstances. The removal of adenoids is preferably done with the patient under the influence of a general anæsthetic. For this purpose ether is to be preferred. The child should be placed in a supine position with the head hanging over the operating table in such a manner that the blood will tend to flow out through the mouth instead of down into the larynx, or a modified Trendelenburg position may be used. The mass may be removed with a Gottstein curette, or one of its numerous modifications, or with the forceps designed by Lowenberg. Should hypertrophy of the faucial tonsils be associated, the latter should be removed while the patient is under the anæsthetic and just before the removal of the adenoids is undertaken.

## DISEASES OF THE PHARYNX.

It is very essential to remember that the pharynx possesses the unique distinction of forming a portion not only of the upper air passages but also of the digestive tract. This renders its mucous membrane very susceptible to influences and conditions which affect that of the digestive tract. Thus, disorders of digestion and assimilation are very apt to be accompanied by pathological changes in the pharynx. The gouty or rheumatic diathesis is prompt to show its manifestations in the pharyngeal mucous membrane. The popular expression "stomach cough," implying a cough originating from stomachal disorder, is, after all, not, in many instances, an improper one to apply to the cough which accompanies a congestion of the pharynx due to digestive derangement. The continuity of the pharyngeal mucous membrane with that of the rest of the respiratory tract leads to its frequent involvement in any conditions which affect the integrity of the latter. Any obstruction to nasal respiration, whether acute or chronic, is apt to be productive of serious inflammatory changes in the pharyngeal mucous mem-

brane. Such nasal obstruction causes the inspired air to pass directly into the pharynx without having been warmed and moistened by previous passage through the nostrils. Consequently, from the air taking up its moisture, the surface becomes dry, congested and predisposed to inflammatory changes. It is this factor fully as much as its continuity of structure that causes the pharyngeal mucous membrane to share, as a general rule, in any inflammatory disorder of the nose or nasopharynx.

## ACUTE PHARYNGITIS.

**Etiology.**—This occurs but rarely as an exclusive entity. It generally coincides with an acute digestive disorder or is an exacerbation of a chronic inflammation of the pharyngeal mucous membrane. Owing to its very exposed position, it is remarkable that the pharynx is not more frequently the site of pathological changes. The commonest cause, however, for an acute pharyngitis is exposure to wet or cold, or rapid changes of atmospheric temperature. It also occurs in conjunction with acute digestive disorders. Excessive smoking frequently excites an attack.

**Symptoms.**— The symptoms are not, as a rule, very marked or severe. There is a "raspy" feeling or soreness, sometimes true pain, in the pharyngeal region, occasionally extending up along the Eustachian tubes. Swallowing is usually painful, and there is more or less cough, accompanied by a small amount of thick muco-purulent expectoration. The attack may be ushered in by chilly sensations, and slight malaise and mild fever usually attend it, as do also occasionally general pains and constipation. On inspection, the pharyngeal mucous membrane is seen to be red and somewhat swollen. At first the surface is dry and glazed, but as soon as secretion is established there is much more discharge. Frequently there is marked prominence of the small bloodvessels on its surface. There is almost always also considerable redness of the fauces and tonsils.

**Treatment.**—In almost every instance it is better to begin the treatment of an acute pharyngitis by free purgation. This is particularly beneficial if we use calomel in divided doses followed by a saline. The salicylates exert an almost specific influence in most attacks. If the patient's stomach is upset, or during the period when calomel is being given, it is better to let him take five grains of salol every two hours in lieu of the more powerful (but at the same time more irritant) salts of salicylic acid. Locally, great relief will be experienced from the use of various lozenges or gargles. If the mucous membrane is very dry and glazed, a lozenge of chlorate of potash is often most useful. If there is reason to associate the attack with the gouty diathesis, guaiacum lozenges should be tried. If the pain is intense, cocaine lozenges will often afford relief. A lozenge containing camphor and menthol is also useful in allaying the severe irritation. Sucking cracked ice lessens the congestion and gives great comfort. Although gargles are not as efficient as direct applications to the parts, nevertheless, a bland antiseptic gargle, such as Dobell's or normal salt solution, is often very grateful. If the congestion of the mucous membrane is very marked, it is well to paint the surface with a strong solution of nitrate of silver (30 to 60 gr. to the ounce, 2 to 4 gm. to 30 cc.). A very strong solution of silver nitrate not only acts as an astringent but is an antiseptic, and to a certain extent an anal-

gesic. The patient should be confined to one room, if not to bed. He should be placed on a light diet, and forbidden to smoke or use alcohol. He should likewise use his voice as little as possible.

## CHRONIC CATARRHAL PHARYNGITIS.

**Etiology.**—This very frequent affection is particularly apt to occur in those whose occupation requires constant use of the voice, hence it is frequently termed "voice user's" or "clergyman's sore throat." In such persons it occurs usually as the result of straining the voice, particularly by using it in a faulty manner or at times when there is some inflammation of the parts concerned. Other local factors are the use of tobacco, and the inhalation of irritant substances such as the fumes of acids or alkalies, and other gases. Chronic pharyngitis frequently results from catarrhal affections of the nose, most generally because of nasal obstruction causing mouth breathing. Where there is considerable dropping of mucus in the back of the throat from nasopharyngitis, the pharyngeal mucous membrane becomes inflamed and irritated not only from the direct action of the secretion upon it, but because of the efforts to expel the mucus, the repeated screatus causing intense congestion of the entire pharyngeal wall.

Chronic pharyngitis is frequently seen in association with chronic diseases of the liver, kidney, and heart, as a result of passive congestion. It is one of the commonest manifestations of chronic alcoholism.

**Pathology.**—In the early stages there is a general hyperæmia. Later, the membrane becomes thickened, and there is marked increase in the connective tissue elements, with the formation of prominent granulations upon the surface. The increase in the connective tissue elements extends to the submucous tissues. The process, as a rule, does not markedly involve the glands in the mucous membrane. In many instances the engorgement of the bloodvessels is the most prominent feature.

**Symptoms.**—The chief subjective symptom is a cough which is irritable, unproductive and easily excited by change in atmosphere. On examination the mucous membrane of the throat is seen to be red and congested with considerable dry, slimy mucus adherent to its surface. The voice is generally quite markedly changed, there being considerable huskiness and the patient being at times apt to lose the voice almost completely. Very frequently chronic catarrhal pharyngitis is to be considered as rheumatic, especially so when the patient complains of a peculiar aching in the throat. A curious complaint is of a frequent desire to swallow; occasionally the act of swallowing is accompanied by pain. There is marked engorgement of some of the bloodvessels.

**Treatment.**—This should first be devoted to the underlying cause. If this is found to be a faulty use of the voice, the patient should be given instruction to correct this. The closest attention should be paid to the condition of the digestive tract. Even if the pharyngitis is not dependent upon a disordered digestion, the latter is apt to be associated with it, and its correction is an important factor. The habits, as regards tobacco and alcohol, should be carefully noted. Locally, an alkaline antiseptic wash, such as Dobell's solution, should be prescribed to be used as a spray. For cleansing purposes it will be found much more efficacious if the upper portion

of the throat be sprayed out through the nostrils in addition to the direct spraying of the pharyngeal mucous membrane. Frequently, gargling with warm salt solution will be found more agreeable and more useful than the use of solutions through the atomizer. The local application of a strong solution of nitrate of silver (gr. 30 to 60 to the ounce) daily, or every other day, is a useful adjuvant. If the patient is gouty or rheumatic, our efforts must be directed toward the correction of the existing diathesis.

## CHRONIC FOLLICULAR PHARYNGITIS.

This is characterized, as contrasted with the preceding, by the marked involvement of the glandular elements in the pharyngeal mucous membrane. This produces a granular appearance which has caused the term "granular pharyngitis" to be used interchangeably with the term "follicular." Its etiology is, in most instances, practically similar to that of chronic catarrhal pharyngitis.

Following attacks of acute infectious diseases, such as scarlet fever and diphtheria, a chronic follicular inflammation of the pharyngeal mucous membrane is quite frequently left. As would be expected, it generally follows severe throat involvement.

**Symptoms.**—The subjective symptoms are usually much more noticeable than in a simple chronic catarrhal pharyngitis. There is generally more cough and the voice is much hoarser. The cough is unproductive, except for occasional sticky masses which are dislodged with difficulty. The pain, which is apt to be a particularly disagreeable feature, is of an aching character, and sometimes very sharp. Upon examination, the posterior pharyngeal wall is seen to be dry and glazed, and of a reddish color; scattered across its surface are numerous prominent granulations. There is usually a scanty amount of mucus present upon it.

**Treatment.**—This must be directed especially toward the correction of any underlying diathesis or constitutional cause. The hygiene of the patient's daily life must be carefully inquired into, particularly as to his habits regarding alcohol and tobacco. If he is a voice user, he should have instructions as to the proper method for its employment. The stimulation of the glandular elements of the mucous membrane to increased activity will be found of greatest advantage. This can be done best by the administration of the iodides internally, and by the local use of stimulating solutions of iodine. These can be advantageously employed in solutions of increasing strength, accompanied with potassium iodide, in glycerine as a medium. Another remedy of service is potassium chlorate, in the form of lozenges to be dissolved in the mouth at frequent intervals. The patient should use a gargle consisting of hot salt solution, or of some alkaline antiseptic solution at frequent intervals, in order to get rid of the disagreeable accumulation of stringy mucus.

## RETROPHARYNGEAL ABSCESS.

**Etiology.**—Suppuration in the retropharyngeal tissues is of very common occurrence in young, healthy children. It occurs but rarely in adults, and, in the few adult cases reported, the infection has been traceable to a pus focus

in the immediate neighborhood of the pharynx, such as spinal abscess, or a carious tooth. In children, retropharyngeal abscess frequently follows diphtheria, scarlet fever, and measles.

**Symptoms.**—The onset is insidious, frequently three to six days elapsing before the attention of the physician is directed especially to the throat. For some days before localizing symptoms present themselves, the child will be obviously ill, as shown by fever, general malaise, and loss of appetite. The first symptom directing attention to the throat is generally pain on swallowing. Very shortly the voice becomes muffled, dyspnœa is soon marked and a dry cough begins. Upon examination a smooth rounded swelling can be detected occupying the postpharyngeal wall and extending downward toward the larynx. In some cases the swelling is seen on the lateral walls of the pharynx, and it is in these instances that the pus burrows downward to the greatest extent. Obstruction to respiration may cause marked cyanosis. The condition is not, as a rule, accompanied by any very marked rise of temperature, generally not above 101° F. In adults, the most prominent symptom is dysphagia, the dyspnœa being not nearly so marked.

**Treatment.**—By the time a retropharyngeal abscess has made itself evident as such, the pus has generally pointed to such an extent that its evacuation by incision is urgently indicated. This can readily be accomplished without a general anæsthetic if the parts are well cocainized. Should pointing not have occurred, it is well to make several incisions into the swollen tissues, as this relieves the pain and frequently prevents further accumulation of pus. Applications of ice to the neck externally will generally afford relief to the pain. Free stimulation with whisky and strychnine is indicated, and after the evacuation of the abscess an iron tonic should be prescribed. If an early incision is not made the pus is apt to burrow, as a rule in a downward direction, and very serious results have been reported. Death has occurred from hemorrhage from the carotid or other arteries, and in several instances from œdema of the larynx.

## LUDWIG'S ANGINA. ANGINA LUDOVICI OR ACUTE PHLEGMONOUS PHARYNGITIS.

This is not frequent, although a number of isolated cases have been reported. It is essentially a deep-seated diffuse suppuration of the submucous pharyngeal tissues, and is due to streptococcus infection.

**Symptoms.**—The attack, as a rule, begins with a chill which is soon followed by intense pain in the throat, difficulty in speaking and swallowing, and sometimes marked dyspnœa. The temperature becomes elevated, sometimes to 104° to 105° F., and the pulse correspondingly rapid. Examination reveals an intense congestion and swelling of the pharynx, generally bilateral and extending downward, frequently involving the epiglottis and adjacent tissues. The throat externally is swollen; the tissues feel hard and tense to the touch.

**Treatment.**—The disease is characterized by great physical prostration, so that free stimulation with whisky and strychnine is indicated from the onset. Locally, cold should be applied. The swollen pharyngeal tissues should be freely opened wherever a purulent focus can be located. In some of the reported cases, tracheotomy was necessary.

### ANGIONEUROTIC ŒDEMA OF THE PHARYNX.

This peculiar affection has in recent years been brought prominently to the notice of the profession by the comparatively large number of cases reported. T. H. Halsted[1] reported recently a number of cases and appended a very full bibliography. The diagnosis at times presents considerable difficulty. The affection occurs in connection with digestive disturbances, usually in persons of neurotic tendencies. It is frequently seen in association or alternating with attacks of urticaria. As a general rule, the appearance of wheals on the pharynx is accompanied by the appearance of similar lesions on other parts of the mucous membrane of the upper air passages. Death from rapidly occurring œdema of the larynx has been reported. The symptoms are a feeling of fulness and pain in the throat. On examination, clear, pellucid swellings are seen, varying from the size of a small pea to a cherry, distinctly circumscribed, and without any associated congestion of the mucous membrane. The wheals may remain for some days, or disappear within an hour or so after making their appearance.

**Treatment.**—The effects of local treatment are but slight. We should direct our efforts to finding what lies at fault in the digestive or eliminating systems. Alkalies administered in large doses have seemed to be of service. The salicylates have been used and in some instances have appeared to be of service. There seems to be in some instances a tendency to spontaneous subsidence of the trouble, cases having been studied in which there was no recurrence after a duration extending over some years.

## DISEASES OF THE TONSILS.

The faucial tonsils are really a large pair of lymphatic glands, the functions of which are but imperfectly derstood As with other lymph glands, they probably protect the organism from infections of various kinds by acting as filters, and by in some way lessening the toxicity of microörganisms which come within their sphere of activity. Although they are, accordingly, beneficent in their activity, the tonsils are very subject to morbid changes. Thus, they frequently become hypertrophied to such an extent as to interfere seriously with normal respiration, and they undoubtedly, under many circumstances, instead of acting as protectors against the invasion of microorganisms, serve rather as portals of entry. The bacterial flora of the tonsillar surface is surprising in its number and variety and many virulent bacteria are found in the crypts.

Morbid changes in the tonsils play a most active part in the etiology of acute rheumatic fever and of the endocarditis and chorea which are seen so frequently in association The tonsils as part of the lymphatic system are subject to involvement in the various disorders of it; thus, hypertrophy of the tonsils is most frequently seen accompanying the condition known as the ' lymphatic diathesis," in which there is a tendency to general enlargement of the lymphatic glands

There are several factors which render the faucial tonsils especially sus-

[1] *Transactions of the American Laryngological Association*, 1905.

ceptible to inflammation. Their location subjects them to constant exposure to the inspired air and contact with food or other things which may be taken into the mouth, and their irregular surfaces with wide open cryptic orifices make it an easy matter to understand the frequency with which they become the site of local infections; in fact, when one considers the number of micro-organisms found upon their surface, it is a wonder that they are not more frequently the site of entrance of organisms. Their close relation to the general circulatory and lymphatic systems causes them to be frequently involved in constitutional disorders.

## ACUTE TONSILLITIS.

Practically every acute inflammation of the tonsils involves both the parenchyma and the follicles of the gland. It is therefore better to consider acute tonsillitis under one head rather than attempt to divide the disease into the parenchymatous and follicular varieties as is sometimes done.

**Etiology.**—The chief predisposing cause for acute tonsillitis lies in hypertrophic enlargement of the glands. Rheumatism and gout are also predisposing causes of great importance. The exciting cause of the attack can almost always be found in exposure to cold or damp.

**Pathology.**—Acute tonsillitis is characterized by congestion of the tonsil with much epithelial proliferation which is especially manifested in the lining of the follicles The desquamated epithelial cells, mixed with the fibrinous inflammatory exudate, accumulate within the follicles and appear upon the surface of the swollen tonsils as white patches. Cultures from these white masses show many bacteria, especially staphylococci and streptococci.

**Symptoms.**—The attack may involve one or both tonsils. It is accompanied by much pain in the throat. This is usually constant in character, and increased by efforts at talking or eating. It frequently extends up toward the Eustachian tube on the affected side. The patient generally experiences great difficulty in phonation. Occasionally the tonsil becomes so swollen as to seriously interfere with the swallowing; there is not apt to be any interference with respiration. Accompanying these local symptoms, the patient usually complains of headache and backache. The attack, as a rule, is ushered in by a chill, or at least by chilly sensations; the temperature soon becomes elevated, generally however not much higher than 102° or 103° F. The tongue is usually coated and the bowels constipated, and there is almost always marked malaise, frequently out of proportion to the objective symptoms

The cervical glands on the affected side generally become somewhat swollen. Opening the mouth is very painful, sometimes so much so as to give great difficulty in the proper examination of the throat. When we examine the throat, one or both tonsils will appear swollen, with patches of grayish-white or white exudate filling the crypts. There is also, practically always, more or less redness of the surrounding tissues.

**Diagnosis.**—As a rule, this presents no especial difficulty. The most serious error is to confuse it with diphtheria. In diphtheria, the exudation which is seen upon the face of the tonsil is of the nature of a membrane, which is closely adherent to the underlying surface. Upon attempting to wipe it off, it will be found very firmly attached, and, if wiped off, the under-

lying surface will bleed; the false membrane is also, as a rule, tinged with blood. The exudate in diphtheria is apt to be found on neighboring structures as well as upon the tonsils; thus, it frequently involves the uvula and the pharynx. Of course, a bacteriological examination is to be relied upon for final decision.

**Prognosis.**—An acute tonsillitis usually subsides in three or four days if promptly and properly treated. The patient may be left in a very weak and depressed condition, indicating the free administration of strychnine and alcohol during convalescence. There are practically no sequelæ, except that frequent attacks seem to increase any hypertrophy of the tonsil already present.

**Treatment.**—The constitutional management is of as much importance as the local treatment. It is wise to give a mercurial purge followed by a laxative salt. In acute tonsillitis the salicylates will be found to exert an almost specific action. The earlier their administration, the more efficient is their action, and they should be pushed to the therapeutic limit. Should there be much fever, one of the coal-tar antipyretics, such as phenacetine, may be combined to advantage. Locally, the crypts of the tonsils should be cleansed of the deposits in them by peroxide of hydrogen applied in full strength with a cotton swab. After the application the throat should be sprayed out with an alkaline wash, and a solution of nitrate of silver (1 to 8), applied to the inflamed area. This should be done daily, and in the interval the patient should be instructed to gargle his throat every two hours with peroxide of hydrogen diluted about one-half its full strength. Frequently great benefit may be derived from lozenges containing guaiacum, chlorate of potash, or benzoate of sodium. A somewhat old-fashioned but excellent treatment is the early administration of drop doses of tincture of aconite, at intervals of half an hour until evidences of the constitutional action are observed. It undoubtedly seems to modify the fever and renders the general disturbance less severe. The patient will derive much comfort from sucking cracked ice, which not only lessens the pain but also the congestion. Externally, cold applied to the throat by means of a coil or ice-bag is grateful.

## PERITONSILLAR ABSCESS OR QUINSY.

The term quinsy should be confined to suppuration of the peritonsillar tissues and not applied to the occurrence of pus within the structure of the tonsil itself. In most cases of quinsy there is more or less involvement of the tonsil in the inflammatory process, but in many instances the tonsil is not invaded at all. There is undoubtedly a close relationship between quinsy and rheumatism, the frequency with which it occurs in association with the latter condition being very marked, so much so that rheumatism may be assigned as one of its predisposing causes. Quinsy is most frequently seen in persons with large or ragged tonsils, the wide open cryptic orifices apparently affording a convenient portal for the entrance of the infective microörganism.

**Pathology.**—Although the pus from a peritonsillar abscess contains many varieties of staphylococci and streptococci, a specific microörganism has not yet been isolated. The abscess generally forms in the loose cellular

tissues immediately surrounding the tonsils, and burrows in various directions, especially into the tissues of the soft palate and downward into those of the pharynx. The loose arrangement of the tissues in this neighborhood facilitates very greatly the spreading of the pus. For this reason, and because of pus naturally following the dependent direction, the abscess usually points downward toward the larynx. Although quinsy most frequently occurs on but one side, bilateral cases are quite often seen.

**Symptoms.**—The onset is usually marked by a chill followed by a rapid rise of temperature (103° to 105° F.). From the beginning the patient complains of intense pain in the throat, a pain that is gnawing and throbbing, much aggravated by attempts at eating and talking, and usually extending up in the direction of the ear on the involved side. With this the patient complains of headache; the tongue is furred and the bowels constipated. Articulation is much interfered with, the patient talking as though his mouth was full. There is almost always great prostration.

**Diagnosis.**—This, as a general rule, presents but little difficulty, though mistakes have been recorded, which make it necessary to observe due caution. Examination reveals the peculiar location and nature of the swelling, and palpation readily elicits fluctuation when pus has once formed Duke reports a case in which a colleague opened an aneurism, mistaking it for a quinsy. This would hardly seem possible with the absence of inflammatory symptoms and if the peculiar pulsation was taken into account. From the sore throats which are associated with the acute exanthemata, the diagnosis should be readily made, considering the location and character of the swelling and the absence of membrane. Tumors or new growths of the tonsils have been confused with it, but in such conditions the acute inflammatory symptoms are wanting.

**Prognosis.**—Although, as a rule, favorable as regards life, cases with a fatal result have been reported. This generally occurs because of the rupture of the abscess into the air passages, with death by asphyxia, although several cases have been reported in which death occurred from hemorrhage, the result of erosion of a bloodvessel. Each attack of quinsy is apt to be followed by recurrences, probably because of an underlying diathesis predisposing to it, or else some local pathological condition favoring infection.

**Treatment.**—In quinsy, as in tonsillitis, the salicylates exert an almost specific action. They should be given as soon as the attack is recognized, and their use continued until the patient is thoroughly under their influence. Their action is greatly aided if they are given in conjunction with an alkali, such as sodium bicarbonate. Alkalies have also locally a beneficial action, and, if the patient is instructed to use an alkaline gargle or take a little sodium bicarbonate into his throat at frequent intervals, it will be found very serviceable. Another remedy, of service internally, is guaiacum. A teaspoonful of the ammoniated tincture of guaiacum given in milk every four hours in many instances certainly seems to modify the attack. It is also used in the form of lozenges. Frequently, aconite is given with the salicylates, and if the temperature runs high, the tincture of aconite may be given, one drop every two hours until the therapeutic limit is reached. The bowels should be opened by the administration of a mercurial, followed by salts.

Locally, the pain is much relieved by the patient sucking cracked ice. He should also be given a spray or gargle of diluted hydrogen peroxide, which

will be found very efficacious in disinfecting the throat. This is especially useful after the abscess has been opened, as it burrows into the tissues and gets at the pus in a way nothing else can. The use of cocaine locally to relieve pain is inadvisable, as its constricting effect upon the bloodvessels is followed by a reaction which renders the pain if anything worse than before it was applied. Externally, cold applied by means of a coil to the neck will be found very grateful. As soon as pointing occurs, the abscess should be opened. As a general thing the incision should be made a little below the point where the uvula and soft palate merge, and it should be done under good illumination, the tongue being kept out of the way by a tongue depressor and the parts having been previously cocainized. The incision should be directed downward and inward toward the median line, in order to avoid opening the large vessels in the neighborhood of the tonsil. After the pus is once evacuated the quinsy generally clears up very rapidly. Free stimulation is indicated during convalescence, owing to the great depression which is generally manifest. After the attack is over, the patient should have his throat examined and any ragged or diseased tissue should be removed in order that the dangers of reinfection may be lessened.

## HYPERTROPHY OF THE FAUCIAL TONSILS.

Enlargement of these structures is very common, and occasionally has no pathological significance. Under certain circumstances, however, it becomes of great importance. In early years they present the ordinary structure of lymphatic glands, lying between the pillars of the fauces. They usually manifest a normal tendency to atrophy about the age of puberty. If they do not spontaneously atrophy at that time, they are liable to become the seat of pathological changes of varying severity. We may recognize two distinct varieties of enlargement of the tonsils, one a true hypertrophy or overgrowth of the gland which is in the nature of a physiological process, the other a hyperplasia of the tonsil resulting from repeated attacks of inflammation with great increase in the amount of connective tissue.

The enlargement of the tonsils which is seen in children is usually of the first variety. The hypertrophy which occurs in adults belongs, as a rule, to the second class. From the above statement, it will be gathered that hypertrophy of the tonsils may arise from several quite distinct sources. Occurring in young persons it is frequently the result of overactivity of a physiological kind. When seen in adults, the hypertrophy may be the remainder of such glandular overgrowth in early life, but with this overgrowth there is usually associated, as a distinct factor, repeated attacks of inflammation of the tonsils, or the latter may be the sole cause which has brought about the increase in their size. There is no doubt that in gouty and rheumatic persons who suffer from repeated attacks of tonsillitis, the tonsillar structure tends to become greatly enlarged as the result of increased blood supply and the constant deposition of inflammatory products. In children, hypertrophy of the faucial tonsils is frequently found in connection with the strumous diathesis, occurring in rachitic and scrofulous children.

**Pathology.**—Probably all tonsillar hypertrophy begins as a simple overgrowth of the tissues which normally compose its structure. After repeated attacks of inflammation the tonsillar enlargement becomes hyperplastic, and

the overgrowth is composed very largely of new-formed connective tissue; accordingly, we speak of the hypertrophied tonsil consisting in an increase in the normal elements of the glands, and of the hyperplastic tonsil consisting of an increase in the glandular elements, combined with the organized products of inflammatory activity. In the hypertrophic form, the tonsil is more or less soft and cuts easily; in the hyperplastic variety the surface of the tonsil is apt to be irregular, with large crypts, and on section it is more or less fibrous and resistant. The surface of the hypertrophied tonsil is generally irregular or even lobular, and the follicles are apt to be widely open and contain much caseous deposit. As a rule, the enlargement of the tonsils is bilateral, although occasionally it occurs only on one side.

**Symptoms.**—Chronic enlargement of the tonsils may exist for many years without giving rise to any notable disturbances either local or general, but usually the mechanical obstruction to respiration produces certain characteristic symptoms. The expression is that natural to the habitual mouth-breather. Consequent upon this mouth breathing, is the development of more or less irritability in the fauces and pharynx, producing an irritative cough, which occurs especially during the night. In children, the sleep is apt to be restless and disturbed, and if the obstruction is very great it may give rise to attacks of nightmare. The voice is materially altered because of lack of nasal resonance. Owing to the accumulation of caseous material within the crypts of the tonsils, the breath is apt to become very offensive. Any enlargement of the tonsil also seriously interferes with the ventilation of the middle ear on the affected side because of the proximity of the gland to the pharyngeal orifice of the Eustachian tube, not only by mechanically obstructing the tube but by its interference with the proper activities of the muscles which control the entrance of air into the middle ear. In addition, the patient with chronically enlarged tonsils is subject, as a rule, to repeated attacks of acute inflammation of those glands. Besides the pain, discomfort and danger attendant upon the individual attack, each one tends to add to the already existing enlargement. The most serious danger is the readiness with which many forms of infection find their entrance into the organism through the enlarged tonsils. The liability to contract diphtheria or scarlet fever is undoubtedly greatly increased by their hypertrophy.

**Treatment.**—This is in reality confined to their removal by some form of cutting instrument, or by electricity. Although many alterative and astringent applications have been recommended with a view to bringing about a reduction in the size of the overgrown tonsil, it is doubtful if any of them possess any real value. For this purpose iodine has been extolled above all other drugs, but although at one time it was greatly in vogue it is now little used. Many astringents, such as glycerol of tannin, solutions of nitrate of silver, sulphate of zinc, etc., have been recommended from time to time but none of them has proved of much use Of the various chemical cauterizing agents which were formerly used, chromic acid and nitric acid were the most popular, but their use cannot be too strongly deprecated, because it is impossible to confine their activities solely to the point which it is desired to affect. The Paquelin cautery has also been abandoned. The galvanic cautery is still occasionally employed in cases in which operative interference is deemed inadvisable or absolutely refused. In order to complete the destruction of the tonsil with it, twenty or thirty sittings are generally required, and the procedure is painful and wearing.

An important point in the technique, if the electric cautery is used, is to be sure the current is off at the time the electrode is applied to the tonsil, and also at the time of its removal from the surfaces cauterized, otherwise unnecessary searing of the surface will result. In cases where much hemorrhage is anticipated in excising the tonsils, it is sometimes advisable to use an electric wire snare. As a general thing, however, these snares are unwieldy, and the results obtained by their use are not very satisfactory.

The most satisfactory method for the removal of the tonsils is undoubtedly to be found in the use of one of the many forms of tonsil guillotine, or tonsillotome. The question of the anæsthetic is an important one. If possible, the operation is always most satisfactorily performed under local anæsthesia, thereby securing the coöperation of the patient, and rendering the manipulation much easier. In children or nervous persons, it is better to use a general anæsthetic, preferably ether. At the meeting of the American Laryngological Association in 1904, the author presented a statistical study of the fatal results of operations upon the nose and throat, in which no less than 21 deaths occurred attributable to chloroform used as an anæsthetic for the removal of tonsils or adenoid growths, as contrasted with but 1 death reported during the administration of ether. When general anæsthesia is used, the patient should be placed in the recumbent position, with the head inclined downward. In this posture the blood is permitted to flow out of the mouth.

Subsequent to the operation, the patient should be confined to bed for at least twenty-four hours, and to his room for several days. For the first twenty-four hours, the diet should consist of cold liquids, or semi-solids, as hot food tends to congest the parts. For pain or bleeding, sucking cracked ice is the most efficient form of relief. An alkaline cleansing spray should also be used at frequent intervals. A point into which careful inquiry should always be made before undertaking any operation for the removal of the tonsils is as to any tendency to hemorrhage on the part of the patient. A number of deaths following tonsillotomy have been reported as occurring in patients who were subjects of the hæmophilic diathesis.

## MYCOSIS OF THE TONSILS AND FAUCES.

This condition is characterized by the presence over the surface of the fauces and tonsils, and in the crypts of the latter, of white masses of granular material and epithelial debris, almost invariably accompanied by the presence of the *Leptothrix buccalis*. In many instances microscopic examination reveals the presence of keratoid material, and many authorities go so far as to consider the process as a keratosis of the epithelium. Others have attributed the condition to the activities of the leptothrix. It is probable that the presence of the latter is more than a coincidence, although it can hardly be regarded as a causal factor, because it occurs in the buccal secretions of almost all persons, whereas the pathological condition of mycosis is one of considerable rarity. There is undoubtedly a very marked proliferation of the epithelium underlying the masses, and the latter have an organic relation to the epithelial surface. It would, therefore, seem that mycotic tonsillitis should be regarded as a proliferative disorder of the epithelial covering of the fauces and tonsils, and that the lesion is frequently of the nature of a keratosis.

The condition occurs in young and otherwise healthy adults; it is very much more common in the female sex. The reason for discrepancy in the sexes is not far to seek, as mycotic tonsillitis is practically never seen in those who use tobacco.

**Symptoms.**—It is rare for mycosis to make itself manifest by any definite symptoms. It is usually accidentally discovered during an inspection of the fauces for some entirely unrelated reason. Occasionally patients complain of slight sticking sensations, especially noticeable during efforts at swallowing, but even this minor discomfort is, as a rule, not complained of by the patient until his attention has been directed to the condition of his throat. Upon inspection the whitish or yellowish-white masses, varying from the size of a pin head to that of a small pea, are readily seen projecting from the surface of the mucous membrane. The spots vary in number, sometimes only one or two can be found, at other times as many as fifteen or twenty. They may extend down on the posterior wall of the pharynx, and a favorite locality for them is in the glosso-epiglottic space, and about the root of the tongue. The masses stick firmly to the surface, and can be removed only with difficulty, generally leaving a small bleeding spot. Mycosis is unaccompanied by any general manifestations, although cases have been reported in which its recurrence in association with digestive disorders has given rise to the supposition that there was some relation between the condition and the disorder of the digestion.

**Diagnosis.**—The disease presents but little difficulty in diagnosis. Occasionally the masses are mistaken for the accumulations which occur in follicular tonsillitis, and there are cases on record in which a mistaken diagnosis of diphtheria was made. Both of these should be readily excluded by careful examination, and, in case of doubt, a microscopic examination of a portion of one patch would suffice to make the diagnosis certain.

**Treatment.**—The fact that this disease occurs only in non-smokers would suggest that the cultivation of the habit of using tobacco would be an easy solution of the difficulty of treatment However, in cases in non-smoking men the development of the tobacco habit has not always been efficacious in curing the complaint So far as local treatment is concerned, the results are very unsatisfactory. It is of great importance to attend to the proper hygiene of the mouth and teeth For this purpose antiseptic mouth-washes should be used, the teeth carefully cleansed, and any dental disorder corrected The patches should be cleansed away as far as possible by frequent application of hydrogen of peroxide, and applications of nitrate of silver or of iodine made to them. In many instances the application of a strong solution of bichloride of mercury will prove of service.

Much can be done by the removal of the masses by diligent scraping with a sharp curette before the applications of the various solutions. Should all minor measures prove ineffectual, it is frequently possible to effect a cure by the application of chromic acid or trichloracetic acid, or by the use of the galvano cautery. In many instances the condition continues in spite of all measures and finally spontaneously disappears.

## TONSILLOLITHS.

The formation of calculi within the tonsils is not very frequent, although it is quite common to find calcareous masses in the caseous material which accumulates so often within the crypts. Tonsil stones are generally the result of calcareous degeneration of the tonsillar secretion which has accumulated in the follicles. They usually give rise to but little disturbance, although the patient may complain of a feeling of fulness in the region of the tonsil in which the stone is located. Their recognition is, as a general rule, easy, although quite frequently they are so deeply situated within the structure of the tonsil that they are only discovered accidentally in the course of a tonsillotomy or some other procedure on the gland. The treatment consists in the removal of the calculus either by the unaided fingers, or by the use of a pair of forceps, accompanied if necessary by the dissection of any tissue which may interfere with its extraction.

# CHAPTER XVI.

## HAY FEVER.

By W. P. DUNBAR, M.D.

**History, Epidemiology, and Etiology.**—John Bostock, a London physician, in the year 1819, described a complaint which attacks certain persons every year, lasts six to eight weeks, and manifests itself as a catarrh of the ocular conjunctiva as well as of the nasal and pharyngeal mucous membranes, beginning with tickling, itching, and burning. With some patients it leads also to asthmatic symptoms. Along with these in some patients other complaints occur. The question whether Bostock's "summer catarrh," now commonly called "hay fever," first arose at that time, is one to which an answer has been sought in vain. Everything, especially the statistics collected at that time by Moebius, indicates that one hundred years ago the disease could not have yet had a wide distribution; even in recent decades hay fever must have still been a comparatively rare disease.

Hay fever is to be considered as a product of modern culture. Working people or members of uncivilized nations are very rarely attacked by it. Hay fever especially attacks individuals who belong to the higher strata of culture, and particularly those who are exposed to intense intellectual strain or excitement. Exact statistics as to the extent of the disease do not exist and must be hard to collect. It can, however, be stated that hay fever has proportionally its greatest distribution in North America and next among the English and Germans. In Germany, England, and North America the disease usually begins toward the end of May, and lasts everywhere for five to eight weeks; in America the disease re-appears annually in August and only exceptionally in the same persons who had been attacked in the spring.

Concerning the *cause*, very divergent opinions have arisen. A detailed enumeration of all the proposed hypotheses would fill books. From the beginning all authors were in agreement on one thing, namely, that the etiological researches would have to consider two important factors: First, that only those persons are affected with hay fever who show a *special individual predisposition* to the disease, as otherwise it could not be explained why the same persons are attacked each year. Secondly, a *definite exciting agent* must exist, which causes a paroxysm in these predisposed individuals. Without such a supposition it would be inexplicable that the disease should begin yearly in each predisposed person at a fixed time, as if "under orders." A clear explanation of the individual predisposition meets with great difficulties, and we will return later to this question. Investigations from the beginning have tended toward the discovery of the exciting agent.

Bostock, and many others after him, believed that the disease is based on a hypersensitiveness of the mucous membranes to *dust, bright light, heat,* or *special odors*. They explained away the fact that such noxious influences

are operative throughout the year, while the disease is associated with a particular season, by assuming that the activity of these substances was suddenly increased by the first heat of summer. Such a conception does not take into consideration that in the United States hay fever appears at a time when the heat of summer is already on the wane. In the year 1831, Elliotson proposed the theory that hay fever is caused by the blossoms of gramineous plants. The *pollen theory* was generally accepted as correct after Blackley had established through numerous researches and experiments that the time of onset coincided with the time when the first gramineous pollen is in the air, and that the manifestations of the disease are most intense when the amount of pollen in the air is the greatest.

Several considerations against the pollen theory were urged. Helmholtz maintained that hay fever is caused by *bacteria*. He soon found many adherents, and about ten years ago the bacteria theory might be considered predominant. When the author began to occupy himself in 1895 with the etiology of hay fever, the study of the then modern literature forced him to believe that hay fever actually was produced by bacteria. The results of his own first researches strengthened this attitude, for during the attack definite bacteria were found on the mucous membranes of hay-fever patients, almost in pure culture, which did not exist in the same persons before or after. All attempts to reproduce attacks with the pure cultures of bacteria isolated were as unsuccessful as those of other experimenters. The advocates of the *bacteria theory* believed that they could explain the periodical occurrence on the assumption that the causative bacteria were perhaps adherent to special pollen, and, therefore, became distributed when the respective plants began to bloom. Such an assumption is not, however, necessary, for it has been shown that certain kinds of bacteria (for example, cholera-like vibrios) appear at certain times of the year and are as regularly absent at other periods.

The fact that the bacteria obtained in almost pure culture from hay-fever patients did not produce attacks of hay fever would not in itself have induced the writer to abandon the bacteria theory, for in other investigations it was also proven that bacteria can in one day completely lose and never thereafter recover an originally intense toxicity. But a puzzling fact was the observation that paroxysms of hay fever appeared suddenly and intensely, and then inside of a few hours or even less completely disappeared. The worst attacks of hay fever occur on railroad journeys. The writer proved, however, that a person can ride on railroads on even very hot days during the hay-fever season through blossoming meadows and rye-fields, as long as the windows and doors of the compartment are closed tight and a handkerchief is held in front of the face; on the other hand, as soon as the windows are opened, severe attacks are induced. From these observations it seemed that the agent sought for must be present in great numbers everywhere in blooming meadows and rye-fields. Finally, the writer proved that even in hay-fever season a person can keep himself free from attacks for weeks by not going out-of-doors and keeping the doors and windows carefully closed. During these experiments the writer could induce an attack within a few minutes by sitting under a certain tree in his garden. This quite uniform result suggested the examination of samples of air taken there during hay-fever time, but these investigations led to no results.

In 1902 the writer observed a thick cloud of dust over fields of blossoming rye, and found that it was formed of rye pollen. That suggested the investigation directly of blooming grasses and stalks of rye. As a matter of interest it may be mentioned that in preceding years competent botanical judges were consulted about how to collect plant pollen in large amounts, and it was advised to spread linen sheets over blooming meadows. The writer would have arrived at this end much earlier if he had known of the researches of Elliotson and Blackley. Unfortunately, as nowadays nearly always happens, he had contented himself with an examination of the recent literature only and learned of the valuable experiments of these authors with grass pollen after the final conclusion of the researches to be described. The author was of the opinion that one could arrive at safe conclusions in

FIG. 25

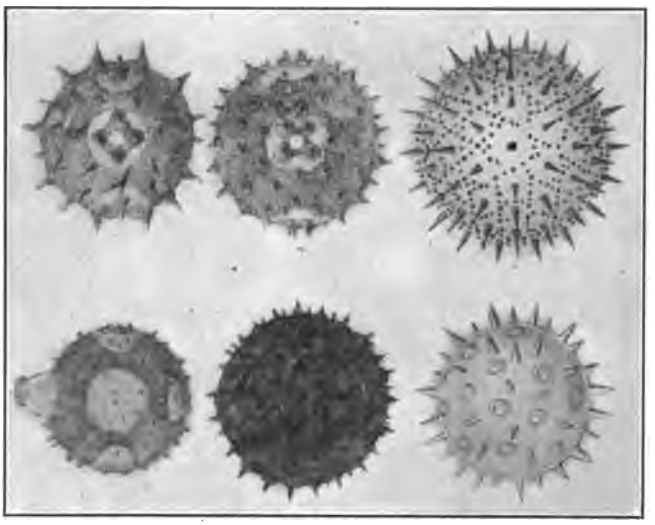
Blossoming rye.

reference to the cause of hay fever *only if it were possible to separate this agent completely from foreign admixtures, especially from bacteria, and if one could produce all the symptoms of hay fever by this agent, independent of temperature and weather conditions, and especially of any particular season, and if finally the proof could be elicited that the agent acts only on those persons who are subject to hay fever, and produces absolutely no symptoms in other persons.*

By means of the pollen of grass blossoms it was possible to produce all the symptoms of hay fever in hay-fever patients. The same material was completely inactive toward normal persons. The pollen first obtained was, however, not bacteria-free. This was obtained by bringing the plant stalks, best of rye and corn, into the laboratory at a time when the yellow anthers had not yet appeared (Fig. 25) and placing them in water in a warm spot.

The anthers then soon appeared, sometimes even within an hour, and it was not long before they began to disseminate a yellow powder. By holding sterile glass vessels underneath, one obtains pollen which is without contamination and completely free from bacteria. Such pure pollen caused attacks of hay fever, but when the experiments were tried somewhat later with the same material on the same patients after the hay-fever season they resulted negatively. Woodward seemed, therefore, to have been right in his conclusion that grass pollen is absolutely harmless outside of the hay-fever season. However, when the experiment was repeated after the membrane of the pollen had been destroyed by treatment in a mortar, it was possible to produce paroxysms in a very short time. With normal persons the ground pollen was inactive, and so the preceding postulates were fulfilled. Even in winter the experiment succeeded with all hay-fever patients who were willing to submit to it, while with normal persons every symptom was lacking.

FIG. 26



Pollen with prickly surface.

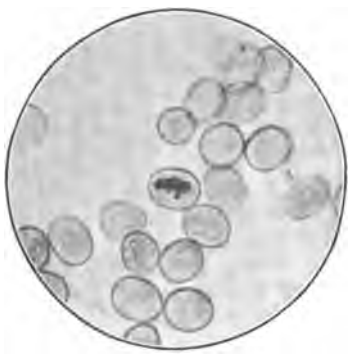
Since the assertion is continually made that hay fever is an imaginary disease and that attacks are brought on in specially sensitive persons merely by looking at a picture of blooming fields, the attempt was made to rule out subjective influences by giving the patient alternately active and inactive material. By these means it was observed that some normal individuals experienced a tingling if merely a drop of distilled water or of normal salt solution were placed on their conjunctivæ. In such instances, however, all objective manifestations were always lacking. Apart from such occurrences, the investigations allowed of only one interpretation, and their correctness was soon confirmed by many observers in England as well as in the United States.

After establishing these facts, experiments were instituted to find out how

the various symptoms, especially the asthma, arise, and whether the hay-fever poison resides in any particular component of the pollen grains.

The next question to be decided was whether a *supersensitiveness of the mucous membranes* is at the bottom of hay fever. Pollen was placed on the mucous membranes by means of little rods or brushes, a method which does not totally exclude the supposition of a mechanical stimulation. Therefore, in order to lay aside this objection the hay-fever patients sat in a glass case into which pollen was dusted; with this method also attacks of hay fever were produced, while normal persons who had placed themselves in the experimental cage at the same time showed no evidence of irritation. It was still an open question as to whether the pollen grains irritated simply mechanically as foreign bodies. Indeed, originally the idea of considering pollen as the cause of hay fever arose from the very reason that the surface of some pollens is thickly covered with spines (Fig. 26). Investigations by the applications of dust, soot, and other foreign bodies showed that hay-fever patients are no

FIG. 27



Grass pollen.

FIG. 28

Starch rods of rye-pollen grains, treated with iodine. × 500.

more sensitive to such things than normal persons. Besides, it could be proven that the pollen of certain plants whose surface is all covered with fine prickles does not irritate hay-fever patients, while the surface of pollen which caused paroxysms is absolutely smooth (Fig. 27). Accordingly, the theory that a purely mechanical irritant was the cause of the attacks had to be abandoned.

Various authors have asserted that certain *odoriferous bodies, ethereal oils*, or similar substances produce hay fever. The widespread conception that hay fever is caused by lime trees and roses may have given rise to this view. The pollen of the limes and roses studied by the writer proved to be totally innocuous to hay-fever patients. But grass blossoms do not smell. It is claimed that sweet vernal grass, *Anthoxanthum odoratum* particularly, must be considered as the cause of hay fever. But the pollen of this grass has no odor. If grass pollen is extracted with alcohol and ether, one succeeds in getting ethereal oils which strongly irritate the mucous membranes

not only those of hay-fever patients, but also of normal persons. They are, however, not felt, because they are present in the pollen in too small amount to be noticed under natural conditions.

Grass-pollen granules are filled with small rods which look like bacteria (Fig. 28). Such rods do not occur in most other plant pollens. The conclusion seemed, therefore, correct that these rods played a part in the etiology. Blackley was of the opinion that the rods in question, whose passage through membranes he believed he had demonstrated, could under certain circumstances pass through the mucous membrane, enter the circulatory system, and so in some cases produce symptoms of hay fever. As a result of previous studies it seemed probable that these rods, which consist of *starch*, really represent the active substance, but with amounts of pollen sufficient to isolate the rods by repeated centrifugalization and to obtain them as a pure white mass, it was possible to demonstrate their complete inertness toward hay-fever patients. Later active plant pollen was found which did not possess the starch granules. In the beginning it was assumed, on the basis of certain investigations, that the so-called starch granules were composed in part of *albumin*. The isolated starch granules proved to be free of albumin. By salting out the crushed grass pollen the writer succeeded in separating the active substance entirely, so that the residue even in large amounts was inactive to hay-fever patients. But from the extract the active principle could be precipitated quantitatively by means of alcohol. The precipitate showed all the reactions of albumin and proved to be active to hay-fever patients in the smallest amounts. In some cases $\frac{1}{40000}$ mg. was sufficient to produce strong objective signs. Normal persons can be subjected to large amounts without any reaction whatever.

It was difficult to accept the view that a well-characterized albumin represented the poison of hay fever. It appeared too new and startling that a chemically pure albumin, perfectly indifferent in its action to most persons, should be for certain individuals such an extraordinarily active poison. Even now no analogy presents itself to my knowledge. It seemed possible that an *enzyme action* might enter into the question. In pollen there are various enzymes, but by chance it was ascertained that grass pollen can completely lose its toxicity without the slightest damage to its enzymes. The recent researches of Kammann on the albumin of grass pollen show that the *pollen globulins* are totally inactive, and that the toxin is attached to the albumin. Pollen toxin is, therefore, a *toxalbumin*. It is absolutely unaltered by heating to 56° C.; at 70 to 80° C. it loses one-quarter of its strength; at 90 to 100° C. three-quarters; at 120° C. it is still active, and is completely destroyed only at 150° C.

With the establishment of the fact that the poison of hay fever is a toxalbumin we had arrived as far in the characterization of the poison as the status of chemical knowledge at that time permitted. Further experiments were naturally easier and more delicate through the possession of the pure toxalbumin, especially in regard to the dosage of the poison. To the objection that one should not work with the isolated poison, but employ fresh pollen extracts in these investigations, it may be stated that the writer considered the work with crushed pollen only as a makeshift until the active principle was isolated, and that it would be a backward step to return to the use of the pollen extracts, which are so easily destroyed and whose doses are so difficult to fix.

One chief objection to the pollen theory has been raised in the fact that comparatively little pollen has been found in successful examinations of air. By the toxin solution obtained it was possible to show that the amount of poison contained in one or perhaps a few rye-pollen grains suffices to produce manifestations of severe irritation in hay-fever patients. During the hay-fever season we were able, by using Blackley's method, to find grass pollen everywhere in the air in very large amounts. Liefmann in Halle, just as Blackley previously in London, found the most pollen in the air on the days that hay-fever patients suffered most. Sometimes as many as 4,000,000 grass-pollen grains settled within twenty-four hours on one square meter of surface. In Halle, Liefmann was able to show that he inhaled about 500 pollen grains inside of twelve minutes, *i. e.*, with each inspiration 2 or 3 pollen grains. Some hay-fever patients could not exist were they to take up such an amount of pollen, if nature did not come to their aid by eliminating a large amount of poison through the mucous secretions before it is dissolved. The observation that individual hay-fever patients suffer before the exact hay-fever time and before the general blooming of grasses was also used as an argument against the pollen theory. Liefmann cleared up this point by proving that as early as April a few grass-pollen grains are found in the air in regions where the general blooming does not appear until several weeks later. In an analogous manner we can explain the appearance of delayed attacks of hay fever by proof of the presence of pollen in the air long after the general blooming period. The fact that hay-fever patients suffer less on *rainy days* has its natural explanation in the demonstrations of Liefmann and Prausnitz that pollen is completely precipitated by rain. At the same time the rain causes a lively formation of pollen in the blossoms, which explains the fact that in a few hours after the cessation of the rain the pollen is soon conveyed in larger amounts to the air. It thus happens that patients even a short time after rain suffer from severe attacks when near blooming grasses. On hot, dry, windy days the paroxysms are most severe and grass pollen is present in the air in greatest amount.

Before the significance of pollen was established experimentally, hay fever in its etiological relations was considered one of the most complicated diseases. The great irregularity which the attacks showed from day to day could not be understood before the proper value was attached to meteorological influences on the increase and diffusion of the causal agent. The hay-fever patient during the time of his attack looks for some external cause for his suffering, and turns his attention directly to striking appearances in his neighborhood. Sometimes it was the bright sunshine, at times dust, now tobacco smoke, the odor of a plant or at times the odor of a cat or a horse, or the influence of a thousand other things; if by chance the same factor re-appeared, the patient immediately thought that his suffering was caused by this factor. For some of the influences in question an explanation can be found. It could be shown, for example, that during the blossoming period many graminaceous pollens settle on roses and other buds; consequently one can produce under these circumstances a severe attack of hay fever by smelling a rose.

In the United States the blossoming of grasses occurs at the same time as in Germany. There they are accustomed to call hay fever also *June cold, rose fever*, or *peach catarrh*. In the United States during the first half of August the same manifestations of the disease re-appear, but in the main

not in those persons who suffered in the spring. The number of those in the United States who suffer in the autumn seems to be much larger than in the spring. Only a few patients suffer from both forms. The duration of the symptoms with these unfortunates is from four to five months.

**North American Autumnal Catarrh.**—After concluding the above experiments it seemed probable that American autumnal catarrh also was caused by plant pollen, but probably from another race of plants. Suspicion had already fallen on *goldenrod* (Solidago) and *ragweed* (Ambrosia), which are everywhere present in the United States as weeds, but are absent in European countries. A ragweed plant was studied which had been taken care of in an herbarium for eleven years. By the pollen of this plant the writer produced typical manifestations of hay fever in such patients as suffered with American hay fever. Further study confirmed the view that ragweed above all else is practically the cause of American autumnal catarrh, and goldenrod to a less extent, because goldenrod does not scatter pollen through the air in such amounts as does ragweed. Active toxalbumin was procured from the pollen of both plants. Finally, it was proven that the pollen of *chrysanthemums* and of all kinds of *asters* have a very poisonous action on patients who suffer from American hay fever, but not on those who suffer only from the spring catarrh.

In connection with the investigations already described we have examined altogether 139 kinds of plants with reference to the activity of their pollen. For spring hay-fever sufferers the pollen of all *Gramineæ* and *Cyperaceæ* that were examined (respectively 25 and 8) were found to be toxic, besides the pollen grains of the following plants:

| | |
|---|---|
| Ligustrum vulgare | = privet. |
| Lonicera caprifolium | = swamp pink. |
| Convallaria majalis | = lily of the valley. |
| Polygonatum multiflorum | = hairy Solomon's seal. |
| Œnothera biennis | |
| Brassica napus | = rape. |
| Brassica acephala quercifolia | = green cabbage |
| Carduus acanthoides | = thistle. |
| Spinacia oleracea | = spinach. |

For autumnal catarrh sufferers the pollen of 11 kinds of plants was found to be toxic, among which are 5 *Ambrosiaceæ* (ragweed) and 2 of the *Solidago* (goldenrod) family besides:

| | |
|---|---|
| Xanthium macrocarpum | = xanthium. |
| Leucanthemum vulgare | = daisy. |
| Centaurea cyanus | = blue bottle. |
| Aster | = starwort. |
| Chrysanthemum | = chrysanthemum. |

**Toxin.**—The symptoms produced by the hay-fever toxin vary with the site of application. By instillation into the conjunctiva one observes itching, tears, photophobia, conjunctivitis with pericorneal injection, up to chemosis. When stronger doses are used a part generally passes through the *ductus nasolacrimalis* into the corresponding nasal cavity and there produces signs of irritation. With nasal applications, sneezing, marked mucous secretion, reddening and swelling of the nose appear; with aspiration of the toxin, severe coughing with expiratory dyspnœa and stridor; with rubbing on the skin, intense itching, local erythema, and wheals.

We have also made *subcutaneous injections* of the pollen toxin. The results obtained were of extraordinary interest, but at the same time terrifying. If a small amount of the toxin was injected subcutaneously in the forearm, the first manifestations appeared in ten minutes, and consisted of severe sneezing, with plentiful secretion from the nasal mucous membranes and considerable swelling of both nostrils; after thirty minutes a dry cough appeared, with a slight, tenacious expectoration, and at the same time the face swelled and became very red and cyanotic. A marked injection of the conjunctivæ developed and later chemosis. In both ears there was a feeling of tension; objectively, however, no change could be perceived in the tympanic membranes. One hour after the injection, tormenting asthmatic disorders with audible stridor arose; an hour later an urticarial-like eruption of large wheals appeared over the whole skin, associated with violent itching; three hours after the injection the forearm began to swell. The œdema spread during the following night to the whole arm. The œdema of the arm and a turgid appearance to the face remained for several days. All other objective phenomena had disappeared by the next morning. The temperature remained normal from the beginning. Nothing abnormal was found in the urine. For a week after the experiment the patient experienced a disturbing sensation of weakness and exhaustion, as well as occasional attacks of palpitation of the heart.. Dr. Carl Prausnitz, who allowed these experiments to be performed on himself, has for many years supported the writer in this work with the greatest devotion, and has always been ready for a repetition of the most unpleasant tests. The author also tried the toxin subcutaneously, with the addition, however, of an antitoxin which at that time possessed only slight power. The injected mixture seemed to be neutral. There were no phenomena at the site of injection, but the toxin was freed in the body. About one-quarter of an hour after the injection itching of the nose and upper lip appeared, with sneezing, lacrimation, and itching of the eyes, followed by weakening of the heart's action almost to the point of complete cessation. Later asthmatic disturbances and urticaria appeared. With a normal person the subcutaneous injection of the same poison produced no specific evidences of irritation.

By the above studies we were able to obtain a comprehensive view as to the origin of the so-called *hay asthma*. This can arise at times after the entrance of the poison into the circulation, and can then be considered a reliable indication of the resorption of the poison. On the other hand, we have also been able to show that the aspiration of the poison can under certain conditions produce asthma. A hay-fever patient who had never suffered from hay asthma suffered from asthmatic troubles after he had talked or laughed in the glass case mentioned above, and in this way had received large amounts of the pollen dust into the deeper air passages. The same patient suffered repeatedly from asthma after handling the extremely finely powdered pollen toxin.

In the meanwhile the pollen toxin has been tried outside of Germany, in the most scattered countries, France, England, Russia, United States, India, Sumatra, and Australia. Everywhere hay-fever patients reacted to the *gramineæ toxin* and at the same time normal persons were unaffected by it. On the basis of this demonstration the writer adopted the view that by means of the pollen toxin the often difficult diagnosis of hay fever could be easily and surely made.

Spring hay fever appears to represent, from an etiological point of view, the same disease throughout the world. But, on the other hand, all patients who suffer from North American autumnal catarrh react to *ragweed* and *goldenrod pollen toxin*, and are almost without exception insensitive to gramineæ toxin. According to this, American autumnal catarrh represents etiologically a disease entity which differs from spring hay fever, but the two diseases stand in close relationship. Whether other forms of hay fever exist cannot with certainty be determined at present. In the cases observed where such a suspicion arose, the question could be decided in the negative. In patients who cannot stand the odor of cats or horses a specific susceptibility to pollen toxin has been shown repeatedly. In Colorado, according to local conceptions, a form of hay fever can be produced by the third blossoming of *alfalfa* (*Medicago sativa*, Lucerne). It has, however, been shown that the affected patients react to ragweed and goldenrod toxin and not to gramineæ toxin. In China a catarrh exists which is attributed to the *privet* blossoms (*Ligustrum vulgare*). It has been proven that privet pollen contains a toxin which has identically the same action as gramineæ toxin. These statements tend to show that to the present no support has been found for the conception of the existence of a third form of hay fever.

Individual observers have obtained no results by the use of pollen toxin. Such observations are explained by the rapid destruction by hydrolysis of solutions of pollen toxin. One should, therefore, employ only freshly made solutions for decisive experiments. Dried pollen toxin stays active for years.

**Antitoxin.**—The author next tried to procure a specific antitoxin in rabbits. These reacted to the poison in different ways. With some the intravenous or subcutaneous injection of the poison gave no noticeable reaction; in others, especially the so-called hares, such reactions appeared as elevation of temperature, loss of weight, and diminished appetite. Some animals died immediately after the injection. Goats appeared to be even less susceptible than rabbits, yet one goat, which had reacted once to the injection of the toxin by attacks of weakness, died immediately after an intravenous injection of pollen toxin. It was the same with horses. Most were absolutely indifferent to the pollen toxin, and yet some horses, and these were nearly always fine animals, reacted strongly to comparatively small amounts of the pollen poison. The susceptible animals gradually became so accustomed to the poison that they could stand fifty times the amount without giving any special reaction.

The blood serum of animals which gave a strong reaction to pollen toxin showed neutralizing properties to the toxin. With a few animals this appeared after a few injections, with others only after regular treatment for months. The antitoxic power of the animal's serum increased in proportion to the immunity to the poison, and obtained a very considerable value after several years' regular continuance of the injections. The standardization of this antitoxin, unlike other antitoxins, cannot be made on animals, but only on hay-fever patients. It is accomplished in the following manner: A solution of the pollen toxin which is sufficient to cause a severe irritation of the mucous membranes of hay-fever patients is mixed with different amounts of the serum to be tested. The mixtures stand an hour at 37° C., then it is determined which of them no longer produces inflammation when instilled on the conjunctivæ of hay-fever patients. If, for instance, the serum in a 30-fold dilution neutralizes this toxin solution, it is given the value of

30 units. During the first year we succeeded in obtaining sera of 20 to 30 units. Now nearly all the horses furnish almost constantly sera of 40 units, the oldest horses even reaching 60 units. If the test solution of toxin is used in sufficient strength we can by our titration method arrive at concordant results even with hay-fever patients of very varying susceptibilities.

By this titration method we have also been able to prove that none of the preparations which have been recommended and produced in imitation of pollen antitoxin can neutralize the pollen toxin. An antitoxin *cannot* be formed in animals by *feeding* them pollen toxin or pollen. Pollen toxin is a *genuine toxin*, just like diphtheria toxin, and differs from this mainly in that it is thermostabile like snake poison. Pollen antitoxin is a genuine antitoxin just like diphtheria antitoxin. All contrary statements, such as have recently repeatedly appeared, lack scientific foundation.

The *specific* treatment of hay fever is more complicated and more difficult than the treatment of infectious diseases, as, for example, diphtheria. With these diseases the patient is only attacked once by the infective agent, and therefore the treatment has only to combat the result of a single infection; but with hay fever the patient comes in contact with the poison every minute for several weeks at a time. Therefore, it must appear from the above that the most rational course is to endeavor to obtain an *active immunization* of patients, *i. e.*, to make them immune to the poison. Investigations on animals have shown that this is possible.

The subcutaneous injection of the poison is accompanied by sequences of the most unpleasant sort and is attended with grave dangers. But gradual active immunization results through the pollen toxin, while we are producing passive immunization. The cause of this lies in the mode of infection just described, *i. e.*, in the fact that every patient comes into contact with the poison annually for weeks at a time. In the case of diphtheria antitoxin and other specific sera, *passive immunity* is obtained by subcutaneous injections. It has been shown experimentally that this method is effectual in hay fever. The effect, however, lasts one day at the most. Therefore, it is necessary to inject the antitoxin daily for several weeks of each year. That in itself is not pleasant, and, moreover, it has specific contra-indications, as follows: it has been shown that some patients are very susceptible to *serum of a different species* and that this susceptibility can be extraordinarily increased by repeated use of the serum. We have to do here with the well-known phenomenon of Theobald Smith, which was further elucidated by Rosenau, that guinea-pigs, after injections of normal horse serum, later prove to be very susceptible to this serum. According to personal observations the same conditions hold for some persons. After the horse serum had been repeatedly injected into the author he became so susceptible to animal serum of every kind that a single drop of any animal serum diluted thirty times with water irritated his mucous membranes intensely. The asserted specific pernicious action of *Pollantin* is connected with this phenomenon. The author sent normal horse serum to those patients who wrote that Pollantin irritated them, and without exception he was told that this irritated them just as much as Pollantin. This hypersusceptibility was manifested especially in those patients who used the serum in unnecessarily large quantities. These patients can gradually become immunized again to the irritating constituents of horse serum by employing Pollantin in a 10 to 20 dilution. The antitoxin is now so strong that traces of serum so diluted

are sufficient to protect against an attack of hay fever, provided it is used *strictly* as a *prophylactic*. The studies of tetanus and diphtheria toxin have shown the great value of prophylactic treatment with specfic antitoxin. If the tetanus antitoxin is injected only one-quarter of an hour later than the toxin, one is forced to use, even then, one hundred times as much antitoxin in order to save the animal as would be necessary were the injections simultaneous. An hour after injections of diphtheria toxin one must use forty times as much antitoxin as would be necessary with simultaneous injections. Experiments have shown that exactly the same conditions exist in hay fever which is of very special importance, but even now comparatively little attention is paid to it.

The pollen antitoxin, Pollantin, must be used daily and repeatedly for a long time. In *liquid form* it therefore requires the addition of a disinfectant, but hay-fever patients are very susceptible to all disinfectants. Even the addition of a very small amount of carbolic acid is not well borne. For this reason the attempt was made to prepare a *permanent* preparation by means of *drying*. The sterile antitoxin is dried in a vacuum and ground to the finest powder. In this dust-like form it irritates the mucous membranes of hay-fever patients. This unpleasant complication is avoided by the addition of sterile sugar of milk. Pollantin is now prepared in two forms; namely, as Pollantinum liqu., *i. e.*, sterile antitoxic horse serum with the addition of ¼ per cent. of carbolic acid, and as Pollantinum pulv., *i. e.*, dried, sterile, pulverized antitoxic horse serum with the addition of sterile powdered milk sugar. Both preparations contain only the additions named. Both articles are prepared for spring hay fever and for North American autumnal hay fever, and are only used after the preliminary determination of their antitoxin value, which at present is higher than is necessary for practical purposes.

**Individual Predisposition.**—Normal persons are absolutely indifferent to the action of pollen toxin. This verifies the correctness of the view, generally held even earlier, that hay fever presupposes an *individual predisposition*. With hay-fever toxin we have for the first time been in a position to conduct experimental investigations on the nature of individual predisposition. During the last few years the author has by means of pollen-toxin investigations aimed at the solution of this problem, but has not arrived at any satisfactory explanation.

When it was demonstrated that the causative agent of hay fever is a soluble toxin and, therefore, an active physiological-chemical substance, most of the hypotheses which had been advanced as to the prime factor of hay fever predisposition fell to the ground. The conception of influences of a purely *suggestive* nature was very broadcast. This view is held by many to-day. It ought to be clear that perceptible, severe signs of irritation of a purely local nature, for instance, on the conjunctiva, cannot be produced by suggestion. Whoever holds this possible should be convinced by investigations, in which alternately pollen toxin and pure water were used, but in which reaction only appeared after the use of the toxin. All explanations to prove predisposition to hay fever a purely *mechanical* affair are made untenable by experiments. One of the most widespread views is that predisposition to hay fever depends on *local obstruction in the nares or the upper air passages* or on *a local damage to nerves*, as, for example, disease of the trigeminus (ethmoidalis) or of the local sympathetic nerve fibers. All these hypotheses

must fall on considering that pollen toxin irritates not only all the mucous membranes of the body, but also the external skin. For a long time it has been believed that the predisposition to hay fever rests on a *gouty diathesis*. Gout is especially prevalent among the Anglo-Saxon peoples just as is hay fever. This theory of a relation to gout still has numerous adherents. This view is not, on the face of it, inconsistent with the pollen theory. Inquiries, however, have shown that gouty persons form only a small proportion of hay-fever patients. Recently, the predisposition has been very generally looked upon as an expression of a *neuropathic disposition*. Hereditary transmission of hay fever is without dispute; nevertheless there seems as much doubt about the neuropathic disposition as of the view of Beard, that hay-fever patients are to be looked upon as *neurasthenic*. *Mental overexertion* is supposed to be of great importance, especially when combined with *responsibility* and *physical overexertion*. In connection with this, it is interesting that inquiries show that the number of men affected is twice as great as the number of women.

Hay fever is said to have occurred frequently as an undoubted sequel of infectious diseases like scarlet fever, measles, diphtheria, pleurisy, and after difficult confinements. The relation which undoubtedly exists between *influenza* and predisposition to hay fever commands special interest. Summing up, one may say that predisposition to hay fever is to be conceived as an expression of a lesion of the nervous system which may be induced by various causes, and is so permanent that spontaneous cures of hay fever are the greatest rarities, and the predisposition is even transmissible. It is remarkable that the predisposition manifests itself by an acquired susceptibility to such a specific substance as the albumin of pollen grains, and further, that hay-fever patients the world over who suffer in spring react to gramineæ toxin, others to the pollen albumin of ragweed and the few other active plants above mentioned, and yet they are totally indifferent to the action of all other plant pollen. The condition seems to be analogous to the *idiosyncrasy* of certain persons to iodoform, antipyrine, shell-fish, strawberries, etc. The view that normal persons gradually develop immunity to pollen toxin can hardly be considered, for, if this were true, Europeans who go to America in the autumn and are inoculated with the ragweed pollen ought to be susceptible to ragweed, for they practically never come in contact with this pollen in Europe. One might think that pollen toxin, which is not a poison in the usual sense of the word, because it does not act on most persons, only becomes a poison when it enters the body of hay-fever patients. Then the secretions of hay-fever patients would have to contain *activating* substances which are lacking in normal individuals. Investigations on this point have given negative results just as attempts to find an antitoxin against pollen toxin in the secretions and blood serum of normal persons have been negative.

In the writer's opinion, the explanation of hay fever lies in a hypersusceptibility to toxin, analogous to that demonstrated by Behring in animals. This hypersusceptibility is probably caused by the pollen itself; for example, in this manner a patient convalescent from influenza meets with a large amount of pollen which he would normally have resisted, but which in his weakened condition produces a permanent susceptibility. In the same way the fact that normal persons working with plant pollen suddenly acquire a susceptibility may be explained. This hypersusceptibility is, however,

not limited solely to the nervous system, but extends also to the *blood corpuscles*. The corpuscles of various hay-fever patients are laked by pollen toxin, while those of all normal individuals tested were resistant to the toxin. The studies have been pursued with numerous persons for several months and always with uniform results.

Pollen toxin is to be considered a poison which has a specific action on the endings of the nerve fibers of predisposed persons. All studies on the explanation of predisposition to hay fever will have to be based on this fact.

**Symptoms.**—The annual attacks appear earlier or later according to the condition of vegetation. The illness commences with slight tickling in the canthus of the eye and in the nose, which comes and goes for about a week and at most results in an occasional fit of sneezing. These slight symptoms increase acutely. The conjunctivæ become œdematous. The patient experiences an uncontrollable tendency to rub his eyes, which feel as if grains of sand were in them. The itching is made worse by the rubbing. The eyes begin to lacrimate copiously and photophobia ensues. Sneezing-fits like explosions occur with considerable secretion of mucus, so that several handkerchiefs may be thoroughly drenched inside of a few minutes. The nasal mucous membranes become œdematous; the nasal passages are occluded. Rhinoscopic examination shows intense injection, especially of the small vessels of the turbinate bodies. The original itching gives way to a sensation of piercing burning. As soon as the patient is compelled to breath through his mouth, the gums and the mucous membranes of the mouth and pharynx begin to itch. An unbearable tickling sensation develops on the soft palate, and later a feeling of rawness, dryness, itching, sticking, and burning appears, which extends from the nose through the posterior nares to the pharynx and Eustachian tubes. Later these symptoms extend to the deeper organs of the throat, and cough with tickling, a scratching feeling of the air passages, hoarseness and a rough voice ensue, until, with a feeling of tension and constriction, shortness of breath begins, which can develop into an asthmatic attack with marked expiratory dyspnœa. Small amounts of tenacious sputum are expectorated, with tormenting straining, and this contains asthma spirals and eosinophile cells. Audible rhonchi soon develop.

The general symptoms may be headache, weakness, exhaustion, depression, ill-humor, languor, tingling in different parts of the body, and an urticarial-like eruption. Digestive troubles also appear in some patients. Some authors claim to have observed albuminuria. If other diseases of the cardiorespiratory system exist at the same time, as tuberculosis or arteriosclerosis, they are made worse during hay-fever time. The plugging of the nose may last for days. As soon as the nose is freed, the patient begins to sneeze, often as much as a hundred times or more at a stretch. After the patient gets over such attacks he feels so exhausted and depressed that he cannot sit up. He does not sleep for nights in succession because of the tormenting symptoms. A condition of the deepest depression arises, often accompanied by suicidal ideas. The patient feels as if he had fever, but no rise of temperature is demonstrable. The disease occasionally shows sudden remissions; the patient feels perfectly well, only to become severely sick again with great suddenness. The attacks appear to be brought on most suddenly by exposure to the open, especially in hot, sultry, windy weather. The remissions are produced most rapidly by staying in-

doors in closed, cool, dark rooms, but also in the open in cool, rainy weather. The suffering usually lasts six weeks. Sometimes, mainly in rainy years, the time may be shorter or it may last eight weeks. The illness disappears as gradually as it arises.

In Italy the disease begins about the middle of April or the first of May, in northern regions toward the end of May or the beginning of June, and about the same time in the northern parts of the United States. In high, mountainous regions it begins later than in the valleys, but all patients in one place are usually attacked on the same day. The remissions and the more severe paroxysms generally strike all patients in the same place at one time. In the United States the illness stops with most patients about the middle of July, but with a few continues to the middle or end of September or even longer. A period of sickness sometimes begins in other patients in the first weeks of August, which has the same course as spring hay fever and also generally lasts six to eight weeks.

Whoever has once had hay fever experiences an attack every succeeding year; usually the attacks become worse each year until the patient is about sixty, when they begin to abate somewhat. It is rare to find hay fever in children; usually it begins at puberty or later. The Caucasian races, especially the Anglo-Saxons, suffer most, and yet the disease is occasionally seen in the yellow and black races.

**Treatment.**—The methods of treating hay fever have been greatly influenced by the conceptions predominant at different times. When local changes in the nasal passages were considered to be at the bottom of the predisposition to hay fever, such obstructions were removed by cauterizing, burning, etc. In the bacteria era, antiseptic washes and salves of bichloride, carbolic acid, and boric acid were used. The adherents of the neuropathic and gouty theories directed their measures to such general complaints. A great variety of drugs have been used. After the patient has tried one remedy after another, he usually turned to narcotics, such as chloroform, morphine, and cocaine. Recently adrenalin preparations in combination with cocaine have been much used.

The adherents of the pollen theory advise patients to stay in closed rooms, especially in regions where there is little vegetation—in the United States, Fire Island, Long Beach, the White Mountains, Green Mountains, the Catskills, and the Adirondacks. Well-to-do patients pass the hay-fever season well at sea. Patients with autumnal catarrh can spend the critical period in Europe without any danger, since ragweed and goldenrod are practically absent. Blackley, even in his day, advised patients who could not leave pollen regions to stop their nostrils with gauze plugs. A series of nose protectors were invented, among which that of Mohr is probably the best known. Curtis advised the internal use of the extract of ragweed for autumnal catarrh.

In view of the paroxysmal character of hay fever and its natural remissions, it is often difficult to arrive at a definite conclusion as to the value of any treatment. Patients are often delighted that hay-fever attacks disappear after the use of a certain remedy. Joyfully they tell their fellow-sufferers about it, forgetting that they only began the use of the remedy when the hay-fever season was about to end. The treatment is further tested with great enthusiasm, only to be absolutely discarded the next year. No lasting results are to be expected from massage cures and various inhalations.

Every patient who has tried the whole series of remedies is always convinced that there is no cure for hay fever.

The introduction of specific serumtherapy brought the first change. The writer has reports of 1240 patients, some of which came from the attending physicians. The results at present are:

I. 696 patients = 56.1 per cent. with excellent results.
II. 381 patients = 30.7 per cent. with partial success.
III. 163 patients = 13.1 per cent. with no success.

In the first group are those patients who, by using the remedy correctly, remained entirely free from attacks or could abort attacks already started. The second group embraces those patients who could alleviate their attacks or some of the symptoms, but could not entirely get rid of them. The cases in which no benefit was derived constitute the third group. These statistics are incomplete in so far as they only comprise results which have come to the writer's personal knowledge. Frequently those who are satisfied with the remedy are not heard from. Those who have attained their object consider the matter as of no importance. Favorable reports seem to have come mainly from those whose occupation was interfered with and whose existence was consequently threatened.

A thorough test of specific serumtherapy in hay fever is very difficult because it takes much larger quantities of antitoxin to combat the fully developed symptoms than would have been required to prevent the onset of the disease. As a rule, only the patient who has full knowledge of the nature of the disease and the mode of transmission of its toxin can be sure of successful results. There are patients who observe no precautions at all, but who, nevertheless, since the use of the serum have had no attack for several years in succession, and during the last year have done well without its use. These patients must be considered as immunized. This immunization must arise from the protection afforded by the antitoxin against very severe attacks which always leave a much increased susceptibility. If this is successful it arises from the fact that a person comes in contact with the poison every year for weeks at a time and absorbs it gradually to the point of active immunization. But if one is exposed to a severe pollen infection before the immunization has proceeded far enough, recrudescences occur. Intelligent patients who follow this plan with sufficient constancy can expect to build up gradually an active immunity. The different stages in the process toward the final immunity are plain, for not only do the attacks become fewer and milder, but a diminished susceptibility to the pollen toxin can be shown experimentally.

Many patients make the mistake of exposing themselves carelessly, by railroad journeys, etc., to the action of the poison. The aim must be to absolutely avoid severe paroxysms, for only in this way can one hope to attain gradual immunity. It is best to sleep with windows closed, thereby excluding the poison for a considerable time. In the morning one should take the antitoxin before arising, so that it can be absorbed before going out and being exposed to infection. The antitoxin is now of such strength that an amount of the powder about the size of a pinhead, or a drop of the liquid serum, placed in each conjunctival sac and a little more in the nose is sufficient. The powder is best applied by insufflation. There is a wide-

spread error of using the serum in excessive amounts, thereby mechanically irritating the mucous membranes and increasing the danger of a hypersusceptibility to the serum.

If the serum is conscientiously employed every morning, then it need be used during the day only when signs of irritation appear, and then in small doses. Too frequent doses are not useful. The mistake of omitting the remedy in the morning after a few days' freedom from attacks is just as widespread. Emphasis is laid on the statement that a patient's condition is set back for some time by every attack which he brings on himself.

The opinion which has lately been repeatedly published, that Pollantin is of value only in light and moderate cases and not in severe ones is not correct. The worst cases get perfectly well under its use and the patients finally become completely immunized. The writer has not yet seen a patient on whom Pollantin had a specific harmful action. It is, therefore, inadmissible to speak of "Pollantin poisoning." Only those patients who are susceptible to normal horse serum are irritated by it. Such persons should use the diluted Pollantin, and only in very small doses.

# CHAPTER XVII.

## DISEASES OF THE LARYNX.

By H S BIRKETT, M. D.

THE signs seen in and the symptoms referable to the larynx which come under frequent observation fall naturally into two classes. The first of these embraces signs and symptoms in the larynx which betoken or accompany disease of the body elsewhere, such as the change of the larynx in aneurism, tabes, syringomyelia, and others which are particularized below. These are apt to be overlooked, are frequently of the greatest diagnostic value, and because they are so diverse do not admit of any more complete classification.

The second class consists of inflammatory diseases of the larynx and certain manifestations of a neurotic origin.

### (A). Laryngeal Signs and Symptoms Referable to Other Diseases.

The importance of an examination of the larynx in many diseases cannot be overestimated, for by means of it a diagnosis which otherwise may be obscure is often made clear at once. It happens frequently that there are no subjective symptoms referred to the larynx, but upon examination very definite signs are found which are of the greatest value. For example, in an obscure case of aortic aneurism the patient's voice may be absolutely clear, but upon examination a complete paralysis of the left vocal cord is found and the explanation of the absence of any subjective vocal symptoms lies in the fact that the non-paralyzed cord may make such compensatory movement as to definitely approximate the paralyzed cord and bring about the condition essential to clear vocal production. This condition the writer has repeatedly seen when the left vocal cord was paralyzed, due not only to aneurism but also to other causes producing pressure upon the recurrent laryngeal nerve, such as an enlargement of the left lobe of the thyroid gland and, rarely, enlargement of the left auricle due to mitral stenosis, pressing the nerve against the aorta and pulmonary artery.

Too great stress cannot be laid upon the necessity for careful examination of the larynx in all cases of enlargement of the thyroid gland, especially when operative interference is contemplated, as an absence of such knowledge has led to unfortunate results, namely, damage to the non-affected laryngeal nerve.

Paralysis of the recurrent laryngeal nerve may follow aneurism of the arch of the aorta, or of the right subclavian artery, or may result from enlarged bronchial lymph glands; and, from the position the nerves occupy in relation to the œsophagus, malignant disease of that organ may produce paralysis of the adductors. In enlargement of either of the lateral lobes of the thyroid

gland the recurrent nerve may be involved and produce paralysis of both adductors and abductors.

The left recurrent laryngeal nerve is more frequently involved than the right.

In aneurism of the arch of the aorta the evidence of its presence is sometimes indicated by distinct pressure upon and visible pulsation of the wall of the trachea. This pressure is in some cases so great as to produce distinct displacement of the trachea, consequent narrowing of the lumen, and accompanying tracheal stridor.

Chronic inflammation of the apices of the lungs, such as tuberculous consolidation and chronic indurative pleurisy, is apt to involve the recurrent laryngeal nerve of either side, but more especially the right one.

In tabes dorsalis, the abductors, as proven by Semon, are especially liable to be affected. This abductor paresis is often a very early sign; it is usually bilateral but may be unilateral. In a patient examined by the writer the only sign was a unilateral (left) abductor paralysis, and in the course of a year he showed definite symptoms of tabes.

In glosso-labio-laryngeal paralysis and in syringomyelia, abductor paralysis is observed. In typhoid fever the vocal paralysis presents no characteristic type, the laryngeal muscles being affected either singly or in groups. The writer has seen the abductors involved in one patient. This is the most common type. "The nature of the paralysis is regarded as a peripheral one, but it is still a matter of dispute whether the muscles themselves, or the peripheral nerves, suffer a pathological alteration" (Friedrich). In chronic lead poisoning either the abductors or adductors may be involved. There is no typical form for the paralysis.

Definite neuritis of the laryngeal nerve has followed influenza or exposure to cold winds, resulting in paralysis of any of the group of intrinsic muscles.

## (B). Inflammatory Diseases of the Larynx.

### ACUTE CATARRHAL LARYNGITIS.

This may occur as a primary affection or secondarily as an extension of a similar condition of the upper respiratory passages.

**Etiology.**—The most frequent cause is an undue exposure to cold or a damp atmosphere. Other causes are: Excessive use of or improper method of using the voice; direct injury to the laryngeal structures or indirect injuries by foreign bodies, either within or in the neighborhood of the larynx; inhalation of irritating vapors, to which those whose occupation compels them to inhale dust, such as bakers, stone-cutters, etc., are particularly exposed; sedentary habits; living in badly ventilated rooms; alcoholic excesses; swallowing of corrosive liquids. The gouty or rheumatic diathesis also predisposes to it. It may occur in any of the exanthemata, especially measles and smallpox; it may arise also during an attack of influenza or typhoid fever. Defective nasal respiration acts as a direct exciting cause.

**Pathology.**—The changes are similar to those of inflammation of mucous membranes elsewhere. The mucous membrane is hyperæmic, swollen and dry looking, especially over those parts where it is loosely attached, such as the false cords and the interarytenoidean space. This is accompanied by the

active production of cell and mucous elements. Sometimes necrosis of the superficial epithelial layer takes place, resulting in slight erosion. This is most frequently met with on the edges of the true cords about the middle third, and is occasionally seen on the vocal processes and the interarytenoidean space. Œdema may follow the inflammatory condition.

**Symptoms.**—In the adult the subjective symptoms are generally very slight. There is a feeling of dryness and irritation of the throat, soon followed by hoarseness, which may increase to complete aphonia. A desire to clear the throat and a dry tickling cough are present with subsequent expectoration of a small amount of clear mucus, sometimes tinged with blood. Usually there is no febrile disturbance. In children, owing to the small size of the glottis and the parts about it being less rigid and resistant than in the adult, the disease is apt to produce rather alarming symptoms, such as dyspnœa, which comes on suddenly accompanied sometimes by the pertussis paradoxus. The temperature in children will range from 100° to 102° F. and objectively the whole laryngeal mucous membrane is hyperæmic, the blood-vessels on the true cords often being quite distinct. Occasionally, minute hemorrhages are to be seen upon the upper surface of the true vocal cords and in some cases superficial erosions occur on the anterior third of each vocal cord. In children suffering from dyspnœa, who will permit a laryngoscopic examination to be made, the mucous membrane below the glottis is found swollen and bulging toward the middle line.

**Diagnosis.**—In the adult the subjective and objective symptoms are quite clear, but it is in children, with whom a laryngoscopic examination is difficult, that a diagnosis is not so readily made. The one condition for which it is apt to be mistaken is laryngeal diphtheria This latter condition is generally associated with membrane deposited elsewhere in the upper portion of the respiratory tract, but without the presense of this condition a bacteriological examination of the secretions from the larynx will remove any doubt.

**Prognosis.**—This is always good in primary cases, but if it be the result of any of the infectious diseases a more guarded prognosis must be given.

**Treatment.**—The patient should remain in a room of an even temperature (65°), preferably in bed. Functional rest is most important. Locally, the use of steam inhalations with the compound tincture of benzoin (1 to 10), for five minutes every four hours is, as a rule, sufficient to relieve most patients. In children, the best method of using steam inhalations is by means of a croup kettle. The application of cold to the larynx externally, by means of an ice-bag or ice-coil, is preferred by some. In order to relieve the cough, which often is troublesome, the following will be found beneficial·

℞

| | | |
|---|---|---|
| Menthol | ʒj | (gm 4) |
| Eucalyptol | ʒij | (gm 8) |
| Ol. menth. pip. | ʒiij | (cc 10) |

Five drops of this should be placed on a respirator and inhaled for twenty minutes every four hours. If there be any febrile disturbance, small doses of tincture of aconite may be given. It is well in most cases to begin with a saline purgative. In children the symptoms of dyspnœa are sometimes relieved by the use of emetics. The application of heat or cold by means of cloths will sometimes relieve an attack. In severe cases when there are signs of respiratory obstruction, intubation is indicated.

## CHRONIC LARYNGITIS.

**Etiology.**—This is usually the result of frequent acute attacks and the causes enumerated under Acute Laryngitis are applicable to the "chronic" form. It is often the result of extension of chronic nasal and nasopharyngeal catarrh.

**Pathology.**—The changes are those of hypertrophy of the mucous membrane, which may be general or local. When affecting the ventricular band, this thickening may be so marked as to hide the true cords; or the changes may be localized to the vocal processes (pachydermia of Virchow), or to the interarytenoidean space. The submucosa is infiltrated with cells and the mucous glands are swollen and distinct.

**Symptoms.**—Subjectively, the most common symptom is the frequent clearing of the throat in order to remove a huskiness of the voice. In singers the voice loses its timbre and there is a sense of fatigue in the region of the larynx after moderate use. The expectoration is usually tenacious in character, small in amount, and expelled in the form of small pellets of a grayish color.

Objectively, the vocal cords have lost their bright white appearance and vary in color from a pale pink to a bright red and are thickened. This thickened appearance of the mucous membrane may be limited to the ventricular band, or distinct thickenings may be seen in the interarytenoidean space. Sometimes this hyperplasia of the connective tissue is limited to the subglottic region (chronic subglottic laryngitis). On the surface of the true cords the mucus may be disposed in small pellet-like masses and upon abduction the mucus is drawn into bands stretching across the glottis from one cord to the other. In long-standing cases there is often a paresis of the adductor muscles and an insufficiency of tension. In public speakers, singers and teachers, small nodular thickenings, situated at the junction of the anterior with the middle third of each vocal cord, are occasionally met with.

**Diagnosis.**—Usually there is not much difficulty in recognition but, as many patients with pulmonary tuberculosis have chronic laryngitis for one of the early symptoms, it is advisable to examine the lungs and sputum of all patients who do not readily improve under local treatment.

**Prognosis.**—As the tendency of most catarrhal affections of the respiratory tract is to return, one cannot give the same hopeful prognosis as in the acute form. In the case of singers and public speakers one must be very guarded.

**Treatment.**—As chronic laryngitis is frequently a sequence of chronic catarrhal affections of the nose or nasopharynx, it is of primary importance that unhealthy conditions of these regions receive attention. All forms of obstruction to nasal respiration should have careful attention. Where there is an increase of nasal and pharyngeal secretion, a cleansing solution consisting of bicarbonate and biborate of soda, in the proportion of 5 grains of each to the ounce of warm water, should be used as a spray night and morning. The laryngeal condition should be treated by astringents applied by means of an atomizer. The following are of considerable value: chloride of zinc, 15 grains to the ounce, and argyrol, 40 grains to the ounce. The application should be made once a day. The use of so-called "dry inhalants" is often of benefit, especially in those patients in whom it is difficult to spray the larynx. Any of the following, either singly or in combination, will prove beneficial.

eucalyptol, oleum pini sylvestris, and terebene; 5 drops should be placed on a respirator and inhaled for twenty minutes three times a day. When paresis of the intrinsic laryngeal muscles exists, improvement is often followed by the local application of the faradic or galvanic current. In public speakers, teachers and singers, absolute rest of the voice is essential and in many persons a faulty method of voice production will require correction. Attention must be given to the general health and the correcting of any gouty or rheumatic diathesis. Change of climate and occupation will greatly assist in the more obstinate cases.

## SYPHILITIC LARYNGITIS.

Syphilis of the larynx may manifest itself in either (*a*) the acquired, or (*b*) the congenital form.

(*a*) **Acquired Syphilis.**—Primary syphilis of the larynx is an extremely rare condition, only two cases having been reported, one by Krishaber in 1877, and the second one by Moure in 1890. The lesions met with in acquired laryngeal syphilis are therefore of the secondary and tertiary type, and, concomitantly with these, cutaneous lesions corresponding to each period are frequently found. The period from the primary infection to the development of general infection, as evidenced in the larynx, varies from eight weeks to three months, but the latter may occur as late as twenty or even thirty years after the primary inoculation. The larynx, from its liability to various forms of catarrhal trouble, is especially apt to show lesions of syphilis on account of the lowered resisting power. From the frequency with which men are exposed, through the variety of occupations of life, to catarrhal conditions of the respiratory passages, they are more liable than women to syphilis of the larynx. There is no relation between the character of either the primary or secondary manifestations and the subsequent tertiary symptoms. In a few cases neither the physician nor the patient himself has been able to detect any evidence of primary infection, and even secondary manifestations may not be noticed, and the only evidence one has that a former infection has occurred is the presence of extensive tertiary ulceration.

**Symptoms.**—*Objective.*—The lesions are of the secondary and tertiary stages. The most common lesions of the secondary stage are: First, erythema; secondly, superficial ulceration; thirdly, a mucous patch; and fourth, condylomata. Upon laryngoscopic examination the mucous membrane will be found either to be uniformly hyperæmic, thus presenting essentially the same appearance as that of an ordinary acute laryngitis; or it may show an irregularity in the distribution of the inflammatory areas, this irregularity being due to interposed areas which are non-vascular, and the whole picture presenting a so-called "mottled" appearance, which, as some authors maintain, is definitely characteristic of secondary syphilis. The areas involved in the inflammatory process are generally the epiglottis and the false and true cords. This inflammatory process may lead to a destruction of the superficial layer of the mucous membrane, in which case there will be seen a small shallow and irregularly shaped ulcer whose surface is covered with a yellowish colored secretion. The superficial ulcers may extend and unite with others and when healed leave a very thin, stellate-looking cicatrix. The occurrence of the mucous patch within the larynx as a feature of secon-

dary laryngeal syphilis is comparatively rare In appearance the laryngeal patch is similar to that which occurs in the mouth. It is rounded, oval or oblong in outline, of a whitish-gray or yellowish color, and surrounded by an area which is very hyperæmic. The localities in which such a patch may be seen are the laryngeal surface of the epiglottis and its edges, the aryteno-epiglottidean and the false and true cords. Condylomata in the larynx appear as rounded or oval elevations with a yellowish-colored surface.

Tertiary syphilis manifests itself in three forms: gumma, ulceration, and cicatricial tissue. These conditions exhibit themselves within a period varying from three to twenty or more years after primary infection. The gumma presents itself as an infiltration varying in size from that of a very small pea to a size sufficient to produce obstructive symptoms. In appearance the mucous membrane covering it may be of a normal or darker hue, elevated above the surrounding mucous membrane, and its base presenting an area of inflammation of a deep rose color. It may be found on the laryngeal surface and edges of the epiglottis, the aryteno-epiglottidean folds, the interarytenoidean space, the false cords and the subglottic region. The lesion is usually single but may be multiple. With the progress of time the gumma undergoes a retrograde metamorphosis, as a result of which it becomes yellowish in color and at last, breaking down, presents the stage of ulceration.

The ulcer thus formed has generally a circular outline, the edges of which are ragged and thickened, a surface excavated and covered with a dirty yellowish-colored secretion, and a base displaying a zone of hyperæmia. If neglected, the inflammatory process may extend to the deeper-lying structures, and a perichondritis, with subsequent abscess formation, necrosis of the cartilage and its exfoliation, may ensue. Perichondritis may, however, occur without ulceration. It is in this stage of ulceration that dangerous symptoms are apt to supervene. Œdema, either acute or chronic, may arise and produce symptoms of marked dyspnœa; or the exfolia ed cartilage may obstruct the respiratory tract; or the loss of the cartilage, especially if it be a portion of the thyroid, cricoid, or arytenoid, may lead to such collapse of the larynx proper as to interfere very materially with respiration. The epiglottis may be involved to such an extent as to interfere with the process of deglutition and allow portions of food to enter the larynx. Fixation of one or both cords, as a result of perichondritis or chondritis, may lead in some cases to a narrowing of the rima glottid s and consequent dyspnœa. Myopathic paralysis of the abductors is not of uncommon occurrence but of very serious moment when present. Finally, hemorrhage may occur and even result fatally, but, fortunately, this happens rarely.

The final step of the tertiary stage is that of cicatrization. The less extensive cicatrization is evidenced by a white stellate scar of varying extent. The results of ulceration and cicatrization of adjacent structures often lead to the epiglottis being bound down to the base of the tongue or to the posterior or the lateral walls of the pharynx. Bands may be stretched across the lumen of the pharynx and by their contraction lead to great distortion of the structures. Adhesions between the vocal cords may result in web-like bands which may involve the glottis to a greater or less degree. The cicatricial process may be so severe as to convert the larynx into a mass of cicatricial tissue with a small perforation in the centre acting as the glottis

*Subjective.*—In the secondary stage they are usually those of a severe acute laryngitis. The voice is husky or may be aphonic, there is a moderate

cough and expectoration of a small amount of tenacious secretion; and, if the epiglottis be involved, deglutition may be painful. In the tertiary stage the symptoms are more pronounced; the voice varies from slight huskiness to complete aphonia. Dysphagia is a more frequent symptom in this stage than in the secondary, owing to the involvement of the epiglottis in the inflammatory and destructive processes. Occasionally food finds its way into the larynx when the epiglottis has been considerably destroyed.

It is in the tertiary stage that sudden œdema is apt to supervene, and it may produce such grave symptoms of stenosis as to necessitate immediate tracheotomy. When a suppurative process is going on in the larynx there is marked general disturbance, the temperature rising from 101° to 103° F. Externally, the perichondritis or suppurative process may be marked by swelling and tenderness over the affected part; with destruction of the cartilage and its exfoliation there is always danger of the exfoliated portion obstructing respiration. The breath, when the disease has reached such a stage, is usually very offensive. The expectoration is muco-purulent in character, sometimes tinged with blood, and it may contain fragments of necrotic tissue.

**Diagnosis.**—It is the diffuse laryngitis of the secondary stage that alone requires differentiation from the non-specific acute catarrhal laryngitis. Objectively, there may be at times, and especially when the inflammation is uniformly disposed, considerable difficulty in deciding which of the two conditions is present. Under such circumstances it will be found that the non-specific form of laryngitis will yield to the usual methods of treatment, while one should always be suspicious of a laryngitis which resists such treatment. A laryngitis which occurs in a tuberculous subject may also resist local treatment, but a careful examination of the patient's general condition and of the sputum will very materially aid in clearing up the diagnosis. It is, however, rather in the ulcerative form of the disease that difficulties in the diagnosis present themselves. The diseases from which syphilis of the larynx in this stage requires to be differentiated are tuberculosis and carcinoma. In tuberculosis the ulcers are apt to be numerous, the outline not so sharp or distinct, the edges less indurated, the surface not so deeply excavated, and the granulations pale and indolent-looking. The mucous membrane of the soft palate, pharynx and larynx, is pale; there is some febrile disturbance, with increased rate of pulse, and the general appearance of the patient is that of anæmia. Smears from the ulcerated areas will often reveal the presence of tubercle bacilli, and an examination of the expectoration will generally give a like result.

It must be borne in mind that the two diseases may co-exist, that an ulceration originally syphilitic may become tuberculous.

In carcinoma the difficulty of a differential diagnosis is much greater; here a new growth precedes the stage of ulceration and it is in this latter condition that the difficulty of a diagnosis so often arises. In carcinoma the disease presents itself as an ulcerating outgrowth more frequently than as a true, deep, excavating ulcer such as is observed in syphilis. The ulcerating outgrowth is more vascular in appearance and the surrounding inflammatory area of a deeper color than that which is seen in syphilis. The progress of a carcinomatous ulcer is much slower than that of a syphilitic one. Other subsidiary points which are frequently considered are, the age of the patient, the presence or absence of enlarged glands and the existence of pain, but these afford very little support to either view.

Microscopic examination of a removed portion is often doubtful in its results, but should always be undertaken. In doubtful cases recourse to antisyphilitic remedies may clear up the difficulty, and yet one must not be too sanguine as to the ultimate results, for iodide of potassium has often the effect of producing absorption of the inflammatory products in cases of carcinoma and thus materially altering the picture presented. One is sometimes confronted with the further difficulty of finding the two diseases (syphilis and carcinoma) co-existing.

**Prognosis.**—The prognosis to be expressed in any given case of syphilis of the larynx depends upon, first, the absence of any other co-existing disease (tuberculosis and carcinoma), second, the extent of the existing lesions, and third, the faithfulness with which the patient will adhere to treatment and advice. In the secondary lesions, recovery usually takes place without leaving any noticeable changes; in the tertiary stage, when the ulceration is present, the progress is usually readily arrested and the function of the larynx interfered with only so far as the destructive process has extended. When cicatrization has occurred, very little improvement is to be expected from therapeutic measures.

**Treatment.**—The treatment of syphilis of the larynx is similar to that of syphilis elsewhere. In the secondary manifestations, mercury, given by inunction, yields by far the most satisfactory results. It must be admitted that at times it is very difficult to carry out this mode of treatment with any degree of thoroughness; and yet, unless this be done, one can hardly hope to secure very satisfactory results. In some cases mercury can be given hypodermically.

Locally, alkaline sprays, such as Dobell's and Seiler's, and sedative inhalations (compound tincture of benzoin), are indicated, and, after the subsidence of the acute stage, applications of weak solutions (1 to 20) of nitrate of silver may be applied to the larynx. When gummata or ulcerations are present, iodide of potassium in increasing doses is indicated. Cleansing the ulcerated area with alkaline and antiseptic sprays and the subsequent application of a solution of nitrate of silver, or the insufflation of iodoform or iodol, will very materially assist in the healing process and lessen the offensiveness of the breath. Vegetations may require the use of the curette, forceps, galvano-cautery, or chromic acid, to hasten their disappearance. Neither general nor local treatment avails when fibroid changes with extensive hypertrophy have already tak n place. Adhesions, fibrous bands or membranes, and stenosis of the larynx, require surgical interference.

When syphilis and tuberculosis co-exist it is generally agreed that the syphilitic element should first receive treatment In all forms of syphilis of the larynx smoking and the use of alcohol in any form should be prohibited.

(*b*) **Congenital Syphilis.**—"Laryngeal affections in congenital syphilis are the most common and characteristic of its pathological phenomena, and invasion of the larynx may be looked for with the same confidence in the congenital as in the acquired form of the disease" (John N. Mackenzie).

The larynx may be involved at any age but the disease more commonly shows itself within the first six months after birth. As to sex it is more frequently met with in the female—in the proportion of three to one (Mackenzie). Three distinct forms are to be met with: In the first, the lesions involve the mucous membrane and the submucosa; in the second, the lesions involve the deeper structures and are characterized by extensive

ulceration rapidly involving the cartilaginous framework of the larynx; in the third form, there is a deposit of dense fibrous tissue leading subsequently to contraction and stenosis.

**Symptoms.**—In the early manifestations of the disease the subjective symptoms are those of an intense laryngitis, the voice being quite hoarse; nothing more than a very marked hyperæmia of all the laryngeal structures is to be observed. The co-existence of cutaneous syphilis is of frequent occurrence. In the second form, the ulceration involving the epiglottis and laryngeal structures is increased and the cry of the child is extremely hoarse and more deeply pitched than in the early stage. The cough is harsh and paroxysmal, leading frequently to an attack of vomiting; deglutition is often difficult. In the third variety the voice is almost aphonic and, in consequence of the lumen of larynx and trachea being considerably reduced, there is marked respiratory difficulty, amounting in some cases to orthopnœa, which may be accompanied by cyanosis and convulsions.

**Diagnosis.**—Early forms of the disease may be mistaken for simple laryngitis, but often there are other symptoms of the inherited form to be seen in the skin and mucous membrane of the mouth and throat. In the more advanced form, the evidence of the disease may be found in the state of the teeth, the condition of the eyes, and the presence of cicatrices about the angles of the mouth.

**Prognosis.**—The prognosis of congenital laryngeal syphilis is always grave, but less so in the early stages when, if the affection be recognized and treated, favorable results may be looked for. In the later forms of the disease, however, even when its true nature is recognized, the treatment seems to produce less effect than it does in the acquired form.

**Treatment.**—The best method of treating this form of infantile syphilis is by the use of mercurial ointment. A small quantity of this should be applied on the walls of the abdomen, and a small flannel binder, also containing a small quantity of the ointment, applied about the body. One must be careful in using mercurial ointments on the skin of very young infants, as, owing to its being particularly sensitive, the application may do harm. Calomel, gr. $\frac{1}{8}$ (gm. 0.008), may be given three times a day for several weeks, or pulv. hydrargyri cum creta, gr. $\frac{1}{4}$ to $\frac{1}{2}$ (gm. 0.016 to 0.03). General tonic treatment should follow the course of mercury.

## TUBERCULOUS LARYNGITIS.

**Etiology.**—The primary cause is the entrance of the tubercle bacillus into the tissues of the larynx. Tuberculous laryngitis may be either *primary* or *secondary*.

Primary tuberculous laryngitis is undoubtedly very rare, there being only 3 recorded cases (Demme, Pogrebinski and Orth).

Secondary tuberculous laryngitis occurs in about 30 per cent. of the cases of pulmonary tuberculosis (Heinze).

**Pathology.**—Three stages usually can be recognized: First, hyperæmia or anæmia of laryngeal structures, associated with an exudate of mucus, pus cells, and desquamated epithelium. Second, a state of infiltration, in which a deposit of minute nodules of diseased tissue, called tubercles, takes place, and is most frequently found in the epiglottis, the arytenoid, epiglottidean

folds, and the interarytenoidean space. The third stage is that of ulceration. The tubercles, containing no bloodvessels, are therefore poorly nourished and break down through the process of caseation. The ulcerations are at first superficial, but through the infection with pyogenic cocci become deeper and more extensive and probably play an important role in the production of perichondritis.

**Symptoms.**—*Subjective.*—These depend entirely upon the seat and extent of the invasion. If the intralaryngeal structures are involved, the only symptom may be alteration of the voice ranging from slight huskiness to aphonia. If the epiglottis or aryteno-epiglottidean folds are involved the chief symptom is dysphagia. Cough occurs which may or may not be paroxysmal, and which is often preceded by a tickling sensation; there is expectoration of a clear or yellowish-colored mucus,—as the laryngeal condition is nearly always associated with pulmonary involvement; shortness of breath is not uncommon; a varying degree of fever (99°–103°–104° F.) and a rapid pulse are often present. Functional aphonia (paresis of the adductors or the internal tensors of the cord), associated with general debility, is occasionally met with in early cases of pulmonary tuberculosis.

*Objective.*—As with the subjective symptoms, these depend upon the stage in which the patient is suffering. In the early or catarrhal stage the mucous membrane of the larynx may be frequently hyperæmic or anæmic. If hyperæmic there is frequently associated with it a marked anæmia of the soft palate and pharynx and, what is almost peculiar to these patients, an extremely irritable state of the throat when a laryngoscopic examination is made.

If the stage of infiltration is present the most frequent areas involved are the aryteno-epiglottidean folds. They are swollen, pyriform in shape, a pale pink or red in color, and the swelling often is so great that they are in contact with the posterior and lateral walls of the pharynx.

The interarytenoidean space, when involved, shows distinct thickening of the mucous membrane, which upon phonation is thrown up into hollow-like projections and if the infiltration be sufficiently large it may prevent the approximation of the vocal cords. The surface of the infiltration is often occupied by an ulceration; springing from its base small granulomata may be seen.

Next in frequency of involvement is the epiglottis, which when uniformly infiltrated assumes a turban shape, and often is sufficiently swollen to prevent a view of the interior of the larynx. It is usually of a red color; the ulcers, which are generally situated on the edge and laryngeal surface of the epiglottis, are deep, and the surface covered with a slough. The ventricular bands may be invaded by a tubercular deposit and become swollen; this generally breaks down and leaves a deep ulceration. The vocal cords may present, in addition to an ordinary acute catarrhal state, an infiltration or ulceration. When infiltrated they are swollen, uneven and hyperæmic. If this be confined to one cord it is strongly suggestive of tuberculosis. Ulceration, when present, occurs most frequently on the edges and over the vocal processes. It may be so extensive as to destroy the vocal cords. The mobility of the vocal cords may be impaired, either from extension of the disease into the crico-arytenoid joint or from involvement of the trunk of the recurrent laryngeal nerve, or some of its branches, by pressure or neuritis.

**Diagnosis.**—Laryngeal tuberculosis is generally associated with advanced pulmonary disease and when such is the case there is usually no difficulty in recognizing the nature of the laryngeal lesion. In a small number of patients the pulmonary disease is not easily detected by physical examination. Here a differential diagnosis is more difficult. The two diseases which may resemble laryngeal tuberculosis are syphilis and carcinoma. The differential diagnosis is discussed under Syphilitic Laryngitis.

**Prognosis.**—This must necessarily be guarded, as the laryngeal lesion is only a local expression of pulmonary involvement and the improvement of local conditions depends very greatly upon the improvement in the lungs.

**Treatment.**—Too great stress must not be laid upon the effect of local treatment in laryngeal tuberculosis. It is undoubtedly influenced by any improvement made in the pulmonary condition.

In the acute catarrhal stage the use of inhalations (compound tincture of benzion, eucalyptol, terebene, 1 to 150) are of benefit in relieving the cough and moderating the amount of expectoration. When infiltration or ulceration is present the local application of lactic acid in glycerine is of benefit. It should be applied by means of cotton wool firmly wrapped on a suitable applicator. The solution at first should be weak (5 per cent.), and, as the patient becomes more tolerant, the strength should be increased to 50 per cent. It is well to apply a 5 per cent. solution of cocaine to the site of application beforehand. The application, to be of any service, should be rubbed in vigorously. The following has been found to give results more satisfactory than any other application:

| | |
|---|---|
| Lactic acid | 50 parts |
| Formalin | 7 parts |
| Carbolic acid | 10 parts |
| Water | to 100 parts |

(R. LAKE.)

Intratracheal injections of guaiacol, menthol, etc., have proved useful when the ulceration is superficial or the infiltration of a moderate degree. This treatment has the effect of alleviating the distressing cough. Of the remedies just mentioned, menthol probably gives the best results. It should be dissolved in olive oil, a 1 per cent. solution being used. The application is made by means of a suitable laryngeal syringe under the guidance of the laryngeal mirror. About 1 to 3 drams (4 to 12 cc.) of the fluid (previously warmed) should be used at each injection. The first injection should be made slowly, on account of a possible spasm of the vocal cords.

Injections of solutions of guaiacol, creasote, or lactic acid, into the submucous tissues when infiltration is present, is advocated, but the writer has not found this method of treatment as satisfactory as those detailed above.

When the epiglottis and aryepiglottidean folds are infiltrated or ulcerated, and dysphagia is a marked symptom, this can be relieved by the insufflation of orthoform (5 grains). The use of this to produce local anæsthesia is preferable to a spray of cocaine, of which the local effects last only a short while and the absorption has a bad effect on the general system. When there is œdema of either the epiglottis or the aryteno-epiglottidean folds, relief to the dysphagia is often obtained by puncturing the swollen tissues with a laryngeal knife under the guidance of the laryngeal mirror.

The question of climate in laryngeal tuberculosis is one upon which authorities differ very much. In England it is the opinion that patients with

tuberculosis do not do well in high altitudes, whilst in Canada and the United States the opposite view is held. Upon this subject Trudeau says· "The very fact that there is a difference of opinion upon the effect of altitude on laryngeal tuberculosis, would tend to confirm the view I expressed, that, *per se*, it has no very defined effect, and that the result in each case is determined more by the many other conditions which go to make up the patient's environment, and which influences his nutrition favorably or unfavorably, and through his nutrition his general resistance to his disease, be it situated in the larynx or elsewhere." In selecting a climate for such patients the absence from irritating dust is of more importance than altitude.

It is advisable that the patient with laryngeal tuberculosis be kept under direct laryngeal treatment. Vocal rest is a very necessary adjunct to the successful treatment of many cases of tuberculous laryngitis and it is "particulariy indicated in cases of inflammatory irritation of the larynx in pulmonary tuberculosis, especially in obstinate catarrh of the larynx, congestion of the vocal cords, relaxation of the ventricular bands, and—in more advanced cases—in circumscribed ulceration of the vocal cords, ulceration in the interarytenoid fold, general infiltration, and in impeded movements of the cricoarytenoid joint. But nothing may be expected of it in those hopeless cases of the last stage in which the whole larynx has become a prey to deep ulceration and partial perichondritis." (Semon.)

## ŒDEMATOUS LARYNGITIS.

Œdematous infiltration of the larynx may occur in two forms: (1) *Primary*, which may be subdivided into (*a*) the non-infectious form—a variety of this subdivision is described by Strübing as an angioneurotic œdema,—and (*b*) the infectious form. (2) *Secondary*.

**Etiology.**—The non-infectious form is caused by local injuries, the action of corrosive liquids, and the internal administration of iodide of potassium, even in small doses. In the angioneurotic form no cause has been found. It occurs in persons of a neurotic temperament and certainly is hereditary, as shown in the remarkable series of cases reported by Osler in 1888. "The peculiarity transmitted must be either a morbid susceptibility of tissue or an inherited peculiarity of metabolism, or both combined" (Osler). Worry, mental excitement, anxiety and fright are doubtless causes. The writer has seen œdema of the uvula and soft palate follow the administration of an immunizing dose of antitoxin. It is generally associated with œdema of the skin. In the infectious form it is due to the action of pathogenic bacteria.

In the secondary form the causes are those diseases which frequently produce a perichondritis: tuberculosis, syphilis and carcinoma, typhoid fever, scarlet fever, measles, smallpox, and gonorrhœa (rare). It may also arise from chronic valvular disease, chronic nephritis, and as a passive congestion from pressure on the veins of the neck.

**Pathology.**—Œdema of the larynx is characterized by a serous infiltration of the submucous cellular tissue. In the traumatic cases it is usually unilateral, involving the epiglottis and aryteno-epiglottidean folds. In its disposition it differs from the secondary form, which is always bilateral or symmetrical. In the infectious form the infiltration is either seropurulent or purulent. Angioneurotic œdema depends upon an increased irritability

of the vasodilator nerves, due either to direct or reflex, central or peripheral disturbance. A spasmodic contraction of the vessels is followed by a paralytic dilatation and stasis or retardation of the circulation; serous exudation then ensues, producing acute œdema (Kocher).

**Symptoms.**—*Subjective.*—The patient usually complains of slight difficulty in swallowing and a feeling of fulness in the throat. The voice becomes husky and, as the œdema increases, it becomes more deeply pitched and inspiration and expiration more difficult and stridulous in character. A distressing and irritating cough is often present. The pain accompanying deglutition often shoots up toward the ears. The swelling of the epiglottis and of the aryteno-epiglottidean folds is often so great that these structures lie in contact with the posterior and lateral walls of the pharynx, and liquids, when taken, not entering the œsophagus, may find their way into the larynx and produce an attack of choking. In the infectious form the local condition is generally preceded by a chill or rigor and followed by a rise in temperature (101° to 104° F.). In this form the sequence of events is rapid and prostration most marked. In angioneurotic œdema of the larynx the symptoms appear suddenly, coming on sometimes during sleep, and may be so severe as to end fatally, as reported by Osler and Griffith.

*Objective.*—Upon examination with the laryngoscope, the epiglottis is swollen and turban-shaped, often so much so as to obstruct the view of the larynx; the aryteno-epiglottidean folds fill up the pyriform sinuses and the mucous membrane is tense and glistening. The false cords, when involved, are swollen and the color of the mucous membrane of a deeper rose color than that covering the aryteno-epiglottidean folds and epiglottis. Owing to the mucous membrane of the true cords being intimately attached to the cords, there is little swelling; but just below the cords (*i. e.*, infraglottic), where the mucous membrane is loosely attached, the œdema shows itself by distinct swellings.

**Prognosis.**—This depends upon the cause and extent of the œdema. In the non-infectious cases it is favorable, but in the infectious forms it is most grave. In the secondary form it depends upon the gravity of the primary lesion.

**Treatment.**—Absolute rest in bed is imperative. The room should be warm and the atmosphere moistened with a steam spray, vaporizing the compound tincture of benzoin (1 to 20). No use of the voice should be allowed. Locally, cold, by means of a coil or ice-bag, should be applied to the neck. The use of small pieces of ice dissolved in the mouth is not advised as by the time it reaches the involved parts the ice has become nothing more than warm water. A spray of adrenalin chloride (1 to 5,000) will often lessen the œdema. Should the obstructive symptoms not abate, the swellings should be punctured by means of a guarded laryngeal knife, guided by the laryngoscope. The throat should be previously rendered anæsthetic by applying a 10 per cent. solution of cocaine. Pilocarpine, given hypodermically (gr. $\frac{1}{10}$ to $\frac{1}{4}$, gm. 0.006 to 0.016) has occasionally proved beneficial.

When the symptoms are not relieved by the foregoing treatment, tracheotomy should be performed without any further delay Intubation is not to be recommended, as the swelling is apt to be so marked as to envelop the opening of the tube when in position.

In angioneurotic œdema, the patients, being highly neurotic, require assurance, and all sources of anxiety and worry should be removed.

## LARYNGISMUS STRIDULUS.

This is a spasmodic contraction of the intrinsic muscles of the larynx leading to closure of the glottis; it may occur either in children or adults.

**Etiology.**—*In children* it occurs most frequently between the ages of six months and a year, seldom after seven years of age, it is more common in males than females. These children are usually ill-nourished, badly developed and often rachitic. Faulty digestion, intestinal parasites, delayed dentition and certain conditions of the pharynx and nasopharynx, such as enlarged tonsils and adenoids, act as causes. In excitable children it may be brought on by violent crying. It is sometimes hereditary.

*In adults* it may occur as the result of irritation of the trunk of the pneumogastric nerve or its branches, from enlarged bronchial glands, mediastinal growths or aortic aneurism; elongated uvula or enlargement of the lingual tonsil. In locomotor ataxia it may occur, constituting the so-called laryngeal crisis. It may also occur as a hysterical phenomenon.

**Symptoms.**—In the child the onset is sudden, coming on during sleep, while the child is playing or during a "fit" of crying. The inspirations are short, frequent, and gradually the stridulous character becomes more marked. In a few seconds the short, stridulous breathing gives way to a whistling inspiration and the attack ceases. The child's face becomes livid, the back and neck are arched, the thumbs flexed upon the palms, the hands on the wrists and the feet flexed and turned inward; consciousness ceases. The spasm may be so severe that the glottis is closed and respiration ceases. The face now becomes of an ashy hue and perspiration breaks out on the forehead. The spasm may last from a few seconds to a minute and, when too prolonged, death ensues. The younger the child the more severe is the attack and the more likely to prove fatal. In the adult the attack is similar although much less severe.

**Prognosis.**—Usually the prognosis is good except when the attacks are severe, frequent, or occurring in a very young infant. A rachitic constitution makes the prognosis less favorable.

**Treatment.**—The condition should be regarded as a local manifestation dependent upon some local or constitutional cause.

*During the attack*, the child should be immersed in a hot bath up to its chin; a small quantity of mustard in the bath will act as a diffusible stimulant. Should the spasm be a severe one, a few whiffs of chloroform will often give relief. If the attack be attended with symptoms of impending death from suffocation, intubation or tracheotomy, preferably the former, should be performed.

*In the interval*, attention should be given to correcting any existing general dyscrasia, especially rickets. Any gastric or intestinal disorder should be rectified and the child placed in the most hygienic surroundings. The administration of general tonics is desirable, especially cod-liver oil, the syrup of the iodide of iron in the strumous subject, and in the rickety child small doses of phosphorus are of great value.

In the adult careful examination should be instituted to ascertain the cause and, if possible, rectify it.

# CHAPTER XVIII.

## DISEASES OF THE BRONCHI.

By A. McPHEDRAN, M.B.

### BRONCHITIS.

**Definition.**—Bronchitis is usually defined as a catarrhal inflammation of the bronchial tubes, but the term is equally applicable to any other form of inflammation. All the layers of the bronchial wall are frequently involved in the inflammatory process.

**History.**—Sydenham is usually credited with having been the first to recognize one of the clinical forms of bronchial inflammation to which he gave the name of *peripneumonia notha;* possibly his work consisted rather in making more clear the knowledge then existing of a disease that had been known to and described by ancient writers. The term bronchitis is not an ancient one; it appears to have been used for the first time in 1814 by Badham, of England. His brief treatise had the effect of widely diffusing the knowledge of the disease, the localization and nature of which was rapidly worked out by Pinel, Bichat, and others. It is to Laennec, however, that the term owes its present wide application to all forms of inflammation of the bronchi. With the aid of auscultation and pathological anatomy, he classified the various forms of bronchitis, described their characters, and differentiated the diseases liable to be confounded with them. His work forms the basis of all subsequent descriptions, and since his time little progress was made until the introduction of bacteriology, which has so greatly altered our views of the etiology and pathogenesis of this as well as of many other diseases. Since then the part played by infection in the production of bronchitis is better understood, and although many points are still obscure, there is little doubt that all forms of the disease are due to, or much altered by, infection; in other words, bacteria play an essential role in many forms of bronchitis, and an important one in all.

**Etiology.**—Bronchitis is one of the commonest of diseases. It occurs with great frequency in the child, the adult, and the aged.

For clinical study it is customary to divide the disease into acute bronchitis and chronic bronchitis. While this classification is highly useful from a practical point of view it does not afford a good basis for the study of the causes. Whether an attack of bronchitis is an acute or chronic one depends as much upon the condition of the bronchial mucous membrane and of the patient's general condition as upon the duration or action of the etiological agent. The same cause may therefore excite in the one case an acute bronchitis and in another a chronic bronchitis.

**The Bacteria of the Normal Bronchi.**—There is much diversity of opinion as to whether microörganisms are present in the normal bronchi. In the upper air passages they are found in great numbers and variety. In the nose they are especially numerous, but grow less as the larynx is approached. The bronchi are therefore not only liable to be infected by the germs in the inspired air, but also and chiefly by inoculation from the upper passages.

The bacteria that have been found in the bronchi are the same varieties as those found in the nose, mouth, pharynx, and larynx. Naturally, of course, they will be liable to infection from the same source—the atmosphere. From the exposed position of the bronchi it is difficult to conceive how they can escape infection. The experiments of many investigators have shown that microörganisms are to be found in the air passages and even in the lung alveoli, and that virulent germs may gain entrance through these passages and infect the whole organism.

Wrzosek has shown that in an animal made to breathe the air laden with a culture, either dry or moist, for fifteen minutes, the microörganism is found in the lungs, in the bronchial glands, and even in the organs of the abdominal cavity.

However, that microörganisms do not find ready entrance to the lower respiratory tract is shown by the frequency with which the bronchial mucous membrane has been found sterile. There is no doubt that the number of bacteria lessen with the diminution in the size of the tube, so that they are rarely present in the small bronchi. Among those who have found the membrane sterile are Bâbes, Claisse, Kilpstein, Thompson and Hewlett, and Gibson and Ritchie.[1] The last-named authors have given a very full account of the literature of the subject.

**Means of Protection of the Respiratory Passages.**—The nose affords the chief protection in normal respiration—"a veritable respiratory sentinel." In passing through its many irregular cavities, most of the solid particles are filtered out. The mechanism by which the microörganisms are arrested is complex, but the chief agents are the leukocytes, which exist in very great numbers in the nasal mucous membrane and possess very active phagocytic properties. The vibratile action of the ciliated epithelium aids in arresting and then expelling bacteria. The nasal mucus of itself is said to possess bactericidal properties. Irritation of the nerves of the nasal mucous membrane may be sufficient to excite sneezing, by which many of the invaders are expelled. In mouth breathing, it should be observed, all these defensive agencies are lost and the air reaches the larynx much less pure than that inhaled through the nose.

After passing the nose the air meets in the pharynx an important line of defense against the entrance of bacteria into the bronchi. The pharynx is very rich in lymphatics and therefore contains many phagocytes.

Notwithstanding all these defensive provisions, it scarcely seems possible that many microörganisms do not enter the bronchi. But even here the means of defense are not wanting; they consist in the action of the vibratile cilia, the protection afforded by numerous layers of epithelium, the abundant mucus with its probable bactericidal action, and the expulsive action of cough. By these means the air is usually rendered sterile before reaching the small bronchi, whose lining epithelium becomes less abundant until, in the smallest ones, it is formed by a single layer of cells affording little protection to the subjacent structures. A further probable defense consists in the rapidity with which microörganisms are taken in by the lymphatics and carried to the bronchial glands. During this time the phagocytes will have exerted their utmost powers of destruction on them.

Bacteriological investigations have shown that in certain forms of bronchitis, microörganisms are the essential agents in the production of the

[1] *Twentieth Century Practice*, vol xxi, p. 215.

disease, while in others they play at least an important part in its development and course. The work in this field of bacteriology is as yet very incomplete. From the exposed position of the bronchial mucous membrane mixed infections are of early and almost constant occurrence; hence the difficulty in determining which bacterial agent is the effective cause in any individual case is very great. French observers have been foremost in this field of research. Among them, Marfan[1] has been one of the most active. He offers a classification of bronchitis based on the bacteriology, making two broad groups: one due to a specific and the other to a non-specific infection. In the specific group the symptoms and lesions are constant and characteristic, so that they can be readily differentiated from all other diseases. The non-specific infections produce lesions of common inflammation and degeneration, with the ordinary symptoms of reaction, and the variety of microörganism exciting the non-specific form of bronchitis can only be determined by bacteriological examination. The two forms of infection have so much in common that their complete separation at present is not possible, yet the attempt to differentiate them is the only rational course.

Marfan's classification founded on these principles is, although imperfect, yet very instructive.

- (*a*) Bronchitis from specific infections: Specific bronchitis (always the result of a recent or remote contagion).
  - Bronchitis of influenza, pertussis, measles, diphtheria, anthrax, plague, tuberculosis, variola, malaria, glanders, syphilis.
- (*b*) Bronchitis from non-specific infections: Ordinary bronchitis due chiefly to pneumococci and streptococci.
  - From endogenous infection (auto-infection).
    - From germs in the bronchi.
      - Chill.
      - Previous specific bronchitis.
      - Chronic affections of lungs, pleura, and mediastinum
      - Inhalations of irritants.
      - Intoxications (iodine, bromine, and cantharidin).
      - Cardiopathia.
      - Albuminuria.
      - Gastro-intestinal affections.
      - Dyscrasias (asthma, hay fever, urticaria, gout, arthritism, lymphatism).
      - Adynamic states (typhoid fever, chronic malaria, cachexia).
    - Auto-infection from other parts.
      - From above
        - Affections of upper air passages.
        - Pyodermia.
      - Metastatic.
        - Gastro-intestinal origin.
        - Septicæmic origin.
  - From ectogenous infection.
    - Contagion by inhalation.

[1] *Traité de Médecine*, tome vi, p. 281 et seq.

**Specific Bronchitis.**—Each form of this variety of bronchitis is due to a specific microörganism. The bronchitis may be the result of a recent or remote contagion; for its development it is necessary for the specific microorganism to gain access to the mucous membrane of the bronchial tubes.

In *influenza, measles,* and *whooping-cough,* the occurrence of bronchitis is nearly constant, and without doubt the respiratory tract is the door of entrance of the initial infection which is conveyed thither in the inspired air. In *diphtheritic bronchitis* the infection extends from the previously infected fauces. My colleague, W. Goldie, has seen 2 fatal cases of diphtheria, without exudate in the fauces, in which there was general bronchitis without membrane formation, but from the secretion pure cultures of the diphtheria bacillus were obtained. Bronchitis from *anthrax* is rare; it arises from aspiration of the spores, which then multiply in focal areas of the mucous membrane. *Tuberculous bronchitis* is dealt with under that heading. The lesions caused by plague bacilli occur in both lungs and bronchi. Usually it is by inhalation that the virus gains access to the organism, and the respiratory tract is then not only the avenue of entrance, but also the seat of the initial disease.

In the four remaining varieties the infective microörganism reaches the bronchi through the blood stream. In *variola* the eruption, if any occurs, is a vesico-pustule and may lead to a false membrane. An intermittent bronchitis may occur in *malaria.* In *glanders* the nodular eruption may be accompanied by a diffuse phlegmasia of the mucous membrane. In secondary *syphilis* there may be a bronchial eruption. It may be added that in *pemphigus* there may be a similar eruption in the tracheobronchial mucous membrane.

**Common Bronchitis or Bronchitis due to Non-specific Infections.**—This form is due to infection by the microörganisms which cause a great variety of affections: in the bronchial secretion are found streptococci, pneumococci, staphylococci, and others. It is rare to find only a single variety in any case of bronchitis; there may be two, three, or more varieties present. It is probable that they are not all of the same importance in any case, but it may be difficult to determine which plays the chief part. As a rule this can be ascertained only by a careful microscopic and bacteriological investigation.

The difficulty in determining the active microörganisms in the secretion is further increased by its contamination while passing through the upper air passages and mouth; notwithstanding the greatest precautions to prevent contamination a great many kinds of microörganisms are usually found. Not infrequently, fewer bacteria are to be found, after death, in the secretion obtained from the bronchi than from the bronchial walls. In capillary bronchitis and in bronchopneumonia often only a single species can be isolated from the pus obtained from the bronchioles.

Of the microörganisms found in the bronchial secretion, the most frequent are the pneumococcus and the streptococcus, either singly, in association with each other, or with other bacteria.

The *pneumococcus* may be found alone, to the exclusion of other bacteria. During epidemics of influenza followed by bronchitis with tenacious purulent secretion, it has been found in great numbers in the expectoration, and has often possessed great virulence. It is also frequently found in the sputum of phthisis, and of capillary bronchitis so often occurring as a terminal

accident in chronic bronchitis. It may likewise be the cause of pseudo-membranous bronchitis.

The *streptococcus* is found in the secretion of bronchitis as the pathogenic organism about as frequently as the *pneumococcus*. It probably always exists in the normal bronchial mucus, but is virulent only in certain forms of catarrh. It is often the only germ present in the capillary bronchitis of infants due to diverse causes, as measles, syphilis, and the cachexia resulting from gastro-intestinal affections. It is usually the active agent in the purulent bronchitis following diphtheria. In all these forms of bronchitis the germ is like the ordinary *Streptococcus pyogenes*. The virulent form that causes erysipelas may invade the trachea and bronchi secondarily, rarely primarily.

The fact that bronchopneumonia is in the majority of cases due either to pneumococci or streptococci, and the frequency with which they are met in the exudates of bronchitis, indicate that they are the chief agents in causing non-specific bronchitis. They cause the benign disease of the larger tubes as well as the more serious infection of the bronchioles, the difference in the severity of the conditions being due partly to the variation in the virulence of the organism and partly to the susceptibility of the membrane on which it develops.

The *diplobacillus* of Friedländer exists in normal bronchial mucus; it is often met with in the exudate of bronchitis, usually associated with streptococci or pneumococci, but it may occur alone as the active pathogenic agent in simple and fibrinous bronchitis.

Many other microörganisms are met with, some of which seem occasionally to be the pathogenic agent causing the bronchitis. Among them are the *Staphylococcus pyogenes, Micrococcus tetragenus, Bacillus coli communis*, and a number of saprophytes.

As these organisms may be found normally in the trachea and larger bronchi, it necessarily follows that either their activity must be increased, or the natural resistance of the mucous membrane diminished, before the inflammatory process can be excited. They may acquire their virulence in other parts of the body, as the skin and digestive tract, and be carried to the bronchi by the blood or the air.

It now becomes necessary to consider the causes that contribute to bacterial invasion by reducing the powers of resistance of the bronchial mucous membrane.

*Cold or Chill.*—Before the bacterial origin of disease was known, cold was regarded as the cause of many maladies, as pneumonia, rheumatism, pleurisy, etc. Although the advent of bacteriology has dispossessed it of the chief role in the causation of these diseases, it still occupies a place second only to the microörganism directly causing the disease; in some of them, such as common bronchitis, the part played by cold is quite as important as that of the microörganism. Acute bronchitis sometimes follows the sudden inhalation of cold air, but this is quite uncommon. It is ordinarily a chilling of the general surface by exposure to a current of cold air that excites the disease, especially if the body is at the time warm and perspiring freely, as after exercise.

Moist air is much more potent than dry air in causing bronchitis and other diseases due to cold, because moisture abstracts heat from the body much more rapidly; hence the chilliness experienced in a cold, humid atmos-

phere. The effect of cold upon the surface is to cause pallor of the mucous membrane by contraction of the vessels through stimulation of the vasomotor nerves. With the continued application of cold, the vessels relax and the pale membrane becomes at first reddened and, later, livid from blood-stasis in the dilated vessels, with an increased secretion of mucus. The application of warmth to the surface, if not too long delayed, restores the vascular tone to the vessels of the bronchial mucous membrane so that it becomes pale again. These effects show how chilling of the body by exposure to a draught after being heated, causes bronchial congestion which only requires the presence of sufficiently virulent infecting microörganisms to cause a bronchitis.

*Climates* and *seasons* have, therefore, the chief influence in causing bronchitis from cold. It is in the climate of frequent sudden variations that we meet with the constitutions that are peculiarly prone to the occurrence of bronchitis. Children and the aged are especially often affected; the former chiefly because the body surface, and therefore the radiating surface, is much greater relatively to the size of the body than that of the adult, while the aged offer less resistance to the depressing influence of cold owing to the slower metabolic processes and the feebler circulation. For similar reasons those of feeble constitutions are easily affected, as the anæmic, the cachectic, and the rachitic; even disturbed digestion and imperfect excretion lower the resistance in some degree. Certain healthy persons show a peculiar susceptibility to cold. In others, the susceptibility is marked on exposure of certain portions of the body, as in getting the feet wet and cold, or in exposing the chest.

That bronchitis is often excited by exposure to cold is borne out by universal experience, but as to the means by which cold acts all are not agreed. That cold is of itself not sufficient to cause bronchitis is shown by the experience of explorers in Arctic regions. Nansen and his associates did not suffer from any of the diseases ordinarily attributed to cold, although the exposure was often extreme. It was only after their return to a temperate, and therefore a germ-laden atmosphere, that coryza, bronchitis, pneumonia, and rheumatism affected them, and, their immunity having been diminished by their long absence, they became very susceptible to these and other infective diseases, and many of them suffered very severely.

The experiences of the members of the recent expedition to the South Sea are even more instructive. Although much exposed to extreme cold and privations they had no catarrhal affections until a bale of clothing was opened for distribution. Almost immediately there was an outbreak of catarrhal inflammation of the respiratory passages from which none of the members of the company escaped. The infective microörganisms had evidently lain dormant in the bale and were set free when the clothing was shaken out. A similar outbreak occurred later when the ship's carpets were taken up and shaken.

It is not necessary to argue, as few will doubt that bacteria are the active agents in causing the catarrhal inflammation even in bronchitis due to chill. Without the depressing influences of the chill the mucous membrane is able to resist the bacteria, but with the paresis of the vasomotor innervation the membrane is reduced to a state of lowered resistance, and its secretion is increased so that the bacteria normally present on its surface or inhaled multiply rapidly, increase in virulence, and cause the inflammation.

The bacteria usually present in bronchitis from chill are the pneumococcus and streptococcus, either singly or associated, but besides these a special coccus has been found in the sputum and considered the active agent, also a microörganism resembling the Pfeiffer bacillus of influenza, and called *Bacillus catarrhalis.*

**Common Bronchitis as a Sequel to Specific Bronchitis.**—Following influenza, measles, etc., common bronchitis frequently develops secondarily, due usually to pneumococci or streptococci; after diphtheria the streptococcus is almost the constant cause of the secondary affection. As the specific infection injures, and therefore reduces the powers of resistance of the mucous membrane, the secondary infection develops and is of frequent occurrence.

**Foreign Bodies and Such Irritants as Dust and Deleterious Gases.**—Foreign bodies, as dust and food debris, entering the air passages may lead to bronchial infection. If they are putrescent, the bronchitis may be fœtid. Certain gases, such as ammonia and chlorine, and the fumes of such acids as nitrous, nitric, sulphuric, and hydrochloric may excite an attack.

**Toxic Bronchitis.**—In their excretion by the bronchial mucous membrane toxic substances cause a rapid proliferation of the glandular epithelium as well as that on the surface of the mucous membrane and an increased secretion of mucus. The epithelium of the mucous membrane becomes more embryonal in character and therefore less resistant to invasion of microorganisms. At the same time the microörganisms ordinarily present multiply more rapidly and increase in virulence, and unless the process is arrested a bronchitis is soon established. The action of iodine is similar, and this accounts for its use as a therapeutic agent. The elimination by the respiratory tract of certain substances of which *iodine* and *bromine* are the most important may excite bronchitis.

**Rhinitis, Pharyngitis, and Laryngitis.**—Bronchitis may be consecutive to inflammation of the upper air passages, as rhinitis, pharyngitis, and laryngitis. The infection may be carried downward by inhalation of the infective organisms. In infants, disease of the mouth may lead to a fatal capillary bronchitis. In many cases there is simultaneous infection of both the upper air passages and the bronchi, as in measles and influenza. Stenosis of the nasal passages, by causing mouth breathing, is apt to lead to bronchial infection.

**Bronchitis Secondary to Heart Affections.**—Among the most frequent causes of chronic bronchitis are disturbances of the circulation due to affections of the heart. It is worthy of note that blood from the bronchi returns to both sides of the heart; that of the bronchial veins to the right heart through the vena cava, while that of the pulmonary veins is received by the left heart. Therefore, inefficiency of action in either side rapidly and markedly affects the bronchial venous plexuses, causing distention of the vessels and hypersecretion, which in turn favors an abundant growth of organisms in the mucous membrane. Hence, bronchitis is present in almost all cases of cardiac affections after the veins become distended from defective circulation.

**Bronchitis of Renal Affections.**—Bronchitis is a frequent complication of diseases of the kidneys and is described as *bronchitis of albuminuria.* It is due to a variety of causes; partly to cardiac weakness always present in advanced renal disease, and partly to the effect of the uræmic poison on the vasomotor nerves of the bronchial vessels, either directly or through the

medulla. The affection has therefore a double origin, cardiac and uræmic. Netter has ascribed the inflammation in all cases to the pneumococcus or the diplobacillus of Friedländer.

Bronchitis is a common complication of *typhoid fever*. The adynamia of this and other diseases of marked prostration favors the occurrence of bronchial infection. Like chill, the adynamia disorders the function of the vasomotor nerves and thus reduces the resistance of the organism so that the bacteria inhaled as well as those already in the bronchial mucous membrane are enabled to multiply, invade the tissues of the wall of the bronchus and cause inflammation. But in the early stage of typhoid fever, before adynamia occurs, bronchitis is a frequent symptom; there is moderate, diffuse catarrh of the larger tubes that often spreads to the smaller tubes, even to the bronchioles. Its causation is uncertain, as the bacteriology is as yet not well studied. It may prove to be due to an organism or to a toxin causing vasomotor paresis. The bacillus of Eberth, however, probably rarely, if ever, causes bronchitis.

Bronchitis is also of common occurrence in various other adynamic and *cachectic states*, as infective endocarditis, cholera, scurvy, diabetes, chronic nephritis, chronic alcoholism, carcinoma, etc. It is very frequent in the cachexias of the infant, whether of gastro-intestinal, tuberculous, or syphilitic origin. These forms of bronchitis are not altogether due to the vasomotor paresis, but also to the enfeeblement of the heart's action.

**Bronchitis Secondary to Chronic Diseases.**—Asthma is, next to tuberculosis, perhaps the most common cause of chronic bronchitis. To appreciate the frequency of asthmatic bronchitis it should be remembered that it is not necessarily preceded by attacks of characteristic dyspnœa. Hay fever should be included with asthma as a cause of bronchitis. It has been said that in both there is an urticaria-like tumefaction of the mucous membrane, with dilatation of the bronchial vessels of varying duration, derangement of secretion, and desquamation of epithelium—a condition that, if of sufficiently long duration, permits the microörganisms to multiply and establish a bronchial catarrh.

It will thus be evident that common bronchitis usually develops from infection by the bacteria normally found in the bronchial mucous membrane or carried down by the inspired air; but the bacteria alone are not sufficient to produce it. To enable them to cause bronchitis it is necessary that the natural resistance of the mucous membrane be reduced, and this may arise from a variety of causes. The bacteria develop under the influences of all the causes which lessen the vitality of the epithelium and leukocytes, alter the secretion of mucus, and cause congestion of the mucous membrane, whether by disturbance of the vasomotor function or by enfeeblement of the heart's action.

**Special Pathology.**—Of the various layers which compose the walls of the trachea and bronchi, the mucous membrane alone is usually the seat of morbid changes. On postmortem inspection there is often singularly little to be seen by the naked eye. There may be more or less congestion of the lungs, and patches of collapsed lobules surrounded by areas of emphysema scattered here and there. The lesions in the mucous membrane are best demonstrated by making a longitudinal section of the trachea and of the bronchi down to those of the smallest caliber that can be divided.

In inflammation of the capillary bronchi their lumen is always found full of pus. In the trachea and larger bronchi the lesions of the mucous membrane occur in irregular areas. These areas are covered with exudate beneath which the membrane may be pinkish or even red, or may show dilated vessels. But owing to the elasticity of the vessel walls, as well as of the bronchi, this hyperæmia may disappear with death. Often there are minute ecchymoses. The inflamed membrane may be thickened and appear velvety from loops of vessels pushing up the basement membrane; it is soft, full of serum, and friable.

At the beginning of the inflammation the mucous membrane is covered by a viscid, transparent, aërated secretion which soon becomes increasingly yellow and opaque from the mingling of an increasing number of pus corpuscles with the mucus. The changes first observed are in the ciliated epithelial cells, which become swollen and their nuclei more apparent. The epithelium which lies between the ciliated layer and the basement membrane becomes altered by the appearance of rapidly proliferated transitional cells and the entrance of many leukocytes, so that the ciliated epithelium is pushed farther and farther from the basement membrane and finally cast off.

Many cells undergo mucoid degeneration and lose their cilia; their layer arrangement soon becomes broken. At the same time many new capillary loops are formed to nourish the highly active epithelial proliferation. If the inflammation is severe the epithelial cells break down early, and, becoming detached irregularly, are cast into the lumen of the tube. Their places are taken by new cells and leukocytes, and these are in turn rapidly cast off.

The mucous glands take part in the process; they are very active, secrete large quantities of mucus, and become distended. If the inflammation has been severe, pressure on the distended glands forces out a droplet of pus or mucopus, composed of cylindrical cells in a state of mucoid degeneration, lymphoid cells, globules of mucus, and a liquid containing filaments of mucin. The mouth of the emptied gland stands open, appearing like an erosion, and the gland cavity is found to contain desquamated epithelium, leukocytes, and granular protoplasm.

The mucous exudate in the early stage comes from the glands and the goblet cells of the surface. Later, the diapedesis is much more active and the mucus acquires a yellow tint from the admixture of the degenerated leukocytes. In very acute processes, many small vessels rupture and the sputum becomes tinged with streaks of blood.

Ordinarily the process is confined to the mucous membrane; it may, however, extend deeper and affect the elastic tissue, the muscular fibers, and the cartilages. If the inflammation is severe, the muscular tissue surrounding the bronchi becomes infiltrated with leukocytes, which interfere more or less with its function; and if the process is of long duration it may so weaken the bronchial wall as to lead to a dilatation which persists for some time after recovery. In cases in which there is much leukocytic infiltration, and the inflammation continues for some time, the muscular fibers may atrophy at certain places and permanent bronchiectasis result. The elastic fibers are subject to analogous changes.

In the capillary bronchi the morbid changes are essentially different, as their structure differs so greatly from that of the larger tubes. They are lined with a single layer of epithelium of cylindrical, cuboidal form. It

desquamates easily and early in the inflammatory process; the lumen of the tubes becomes filled with purulent exudate, made up of exfoliated epithelium, many leukocytes, and great numbers of microörganisms. The bloodvessels become greatly dilated and surrounded by leukocytes, which also infiltrate the adjoining tissue, and the process soon invades the pulmonary alveoli. The bronchial lymphatics beneath the basement membrane are distended with small cells. This cell infiltration extends to the larger lymphatics, and thence along the perivascular and peribronchial lymphatic trunks to the root of the lung, where in severe cases the glands are found much congested and swollen. The inflammation impairs the strength of the muscular coat of the bronchi, and this may lead to bronchiectatic dilatation.

In fatal cases the right side of the heart is dilated and in chronic ones its walls may be hypertrophied. The veins discharging into the right heart are dilated, and the liver and other organs drained by them are congested.

In *chronic bronchitis* the morbid changes occur most frequently in the upper part of the bronchial tree, rarely in the small branches, and never in the capillary bronchi. The mucous membrane is of a violaceous, gray, or slaty hue; it is thickened from chronic œdema, or by the irregular formation of fibrous tissue, and presents many small papillary outgrowths.

The mouths of the mucous glands are dilated and quite easily seen. In the milder cases the epithelium becomes altered so as to consist of irregularly cylindrical or ovoid cells; it may be formed of only a single layer, or of several irregular layers of cells of varying forms, but chiefly goblet cells that have undergone mucoid degeneration. The surface of the mucous membrane is covered with transparent gelatinous mucus, in which may be seen small, white masses—the perles of Laennec.

In the more severe forms of chronic bronchitis in which the secretion is markedly purulent, the epithelium is replaced by a single layer of ovoid cells placed perpendicularly to the basement membrane. The glands participate in the inflammation and present changes similar to these in the acute disease. Their walls are œdematous, in places infiltrated with round cells and in other parts the seat of fibrinous thickening. Later they atrophy and are replaced by fibrous tissue. The bloodvessels are dilated and tortuous, and show many new capillary loops. In the muscular coat there is irregular, round-celled infiltration separating its fibers. The cartilages usually become gradually absorbed, but they calcify occasionally, converting the bronchus into a rigid tube. They are said to become ossified in rare cases.

There may be more or less dilatation of the bronchi, the lungs are always more or less emphysematous, and the right heart may be dilated.

**Symptoms.**—There are two cardinal symptoms of bronchitis which are never wholly absent—cough and expectoration; and two accessory and inconstant ones—dyspnœa and thoracic pain.

**Cough.**—Cough is the foremost symptom. It is never absent; it may be very slight, or extremely severe and of a loud, ringing character. It may occur as isolated coughs succeeding each other with greater or less frequency, or in paroxysms which may be of great severity and end in vomiting. The severity of the paroxysms is most marked in those of a nervous temperament. At first the cough is dry, and continues so until the hyperæmia of the bronchial mucous membrane gives rise to increased secretion. The irritation causing the cough is often referred to the part of the trachea beneath the sternum; this area feels raw or tender, or there may only be a

vague sensation that cannot be localized. Paroxysms of coughing are often excited by changes of temperature, especially by cold, moist air, and by excitement. The cough is usually worse at night, as the recumbent position causes the secretion to gravitate to the posterior walls of the bronchi, and these are the most sensitive parts.

The object of cough is the expulsion of accumulated secretion from the air passages; but cough is a reflex act, and may be excited by irritation of many peripheral areas, such as: (*a*) *Irritation of the larynx.* (*b*) *Irritation of the mucous membrane* of the *trachea*, especially at its extremities, near the larynx, and at the bifurcation, excites cough, the posterior wall being more sensitive than the anterior. (*c*) *Irritation of the bronchial mucous membrane* causes cough; its sensitiveness diminishes with the lessening in the size of the tubes, practically disappearing as the alveoli are approached. Severe cough therefore occurs only when the larger tubes are affected. (*d*) *Pleural irritation* occasionally causes cough, probably through reflex influence. In the majority of cases of pleurisy in which there is cough there is probably a co-existing bronchitis. Irritation of the costal pleura with a sound during operation for empyema has produced a violent cough (Eichhorst).

*Affections of the lung tissue* do *not* cause cough. It is not until the exudate into the alveoli is forced up into bronchi of a certain caliber and irritates the mucous membrane that cough is excited.

In cases of extrathoracic irritation the cough is feeble and inconstant and varies in different persons.

Cough may be absent in the bronchitis of adynamic states, as typhoid fever, old age, and the cachexias of children; in such cases the secretion accumulates in the bronchi and constitutes a grave condition.

As the secretion becomes copious and liquid, the cough is easier but may be frequent. It may be severe in the morning, as the secretion accumulates during sleep, becomes disturbed on waking, and excites paroxysms of coughing.

**Expectoration.**—Next to the cough, this is the most important symptom of bronchitis; it is never wanting except in occasional cases of dry, chronic catarrh. It is difficult to obtain sputum in young children, in old people, and in the very weak, all of whom usually swallow it.

The *expectoration* of bronchitis is *mucous, muco-purulent, or purulent, rarely serous or pseudo-membranous.*

*Mucous expectoration* occurs in acute and in certain forms of chronic bronchitis. It is scanty, translucent, viscid, and expelled with difficulty. It consists of clear fluid, chiefly mucus, and contains a few white and red blood corpuscles, and some bronchial epithelium, both ciliated and cylindrical. It represents the *sputum crudum* of older writers. As the secretion increases, the sputum becomes more liquid and more easily expelled, so that the cough becomes "looser." It is somewhat frothy, resembling the white of egg containing air bubbles. It may contain streaks of blood from rupture of bronchial capillary loops.

*Muco-purulent Expectoration.*—In the second period of acute bronchitis, owing to the increasing number of leukocytes which pass into the secretion, the sputum gradually becomes yellowish, opaque, and thick—muco-purulent sputum. The changes correspond to those occurring in the secretion of an ordinary nasal catarrh. In the majority of cases of chronic bronchitis, also, the sputum is of a similar character. The sputum may consist in some

parts of transparent mucus; in others, of opaque, yellow, or green purulent masses. Sometimes the purulent parts are distinct, forming nummular or globular masses in the bottom of the sputum cup. These are frequently seen in phthisis. Microscopically the sputum is distinguished from mucous expectoration by the great abundance of pus corpuscles.

*Purulent Expectoration.*—This form is rare and resembles the pus of an abscess; it occurs in some cases of capillary bronchitis and in chronic bronchitis in which there is dilatation of some of the bronchi. On standing, it separates into an upper, transparent layer, and a lower one of thick, greenish ous. If the cough is severe there will also be a frothy layer lying on the surface. Purulent sputum is met with only when there is very marked diapedesis of leukocytes, the complete desquamation of epithelium and destruction of the glands accounting for the absence of mucus.

*Serous* and *pseudo-membranous expectoration* will be referred to under Bronchorrhœa and Fibrinous Bronchitis, respectively.

**Dyspnœa.**—This is not a frequent symptom. The degree of dyspnœa depends on the obstruction to the movement of the air in and out through the tubes caused by the swelling of the mucous membrane and accumulation of secretion. The effect of the obstruction is partly overcome by more rapid breathing; if this is not sufficient the accessory muscles are called into play, and to enable them to act better the patient sits up (orthopnœa). Such difficulty in breathing occurs only when the smaller tubes are affected, or when there is some accessory cause, as emphysema, cardiac disease, etc. In these severe cases there is also inspiratory retraction of the lower part of the chest and of the epigastrium. Riegel has pointed out that in affections of the bronchioles the dyspnœa is chiefly expiratory. Inspiration may be quite free and is never alone affected, as is so often the case in laryngeal disease.

**Pain.**—Pain is not usual in bronchitis. Soreness is often referred to the substernal region, especially on coughing, when the trachea and large bronchi are affected. If the cough is severe, there may be much muscular pain, chiefly at the costal margin and in the epigastrium—that is, at the attachment of the diaphragm and abdominal muscles.

**General Symptoms.**—The general symptoms of bronchitis are: a moderate fever, a slightly quickened pulse, headache, thirst, loss of appetite, coated tongue, generally constipation, and scanty, high-colored urine. The temperature rarely rises above 101° or 102° except in children, in whom it may be high for a day or two only. The skin is at first dry, but later there is usually free perspiration, which, however, does not necessarily bring relief. The perspiration is not a *sleep sweat*, but may occur during the waking hours as well, especially after coughing. It is cold and clammy in the collapse stage.

*The physical signs* are few and nearly wholly auscultatory, such as rhonchi, sibilant rales, and crepitation. Expansion of the chest is generally unaffected, but if there is considerable bronchial obstruction, lateral expansion may be defective, and there may be retraction of the lower part of the thorax. In chronic catarrh of the lower lobes in men, a feminine type of respiration develops (Riegel).

On *palpation*, rhonchial fremitus may be felt when adherent mucus lodged in the larger tubes is displaced by the respiratory movement. The percussion note may be hyperresonant in parts, especially over the margins

of the lungs overlapping the base of the heart and great vessels. There may be dulness at the base due to collapse, congestion, and œdema.

*Auscultation.*—The breath sounds in well-marked cases are harsh, with some lengthening of expiration. Absence of sounds may be found in case of obstruction of the bronchi or collapse of lobules. Sibilant and sonorous rhonchi are the typical signs. They are due to irregular narrowing of the caliber of the smaller and larger bronchi, respectively. The larger rhonchi often disappear or shift their position during coughing, but the finer ones are usually unaffected even by violent coughing.

As the secretion becomes more liquid, moist rales are produced in the tubes, due to the liquid being driven back and forth by the air currents. In the larger tubes they may disappear after coughing, but soon re-appear. The volume of the rale is in proportion to the size of the tube in which it is generated. The large moist, bubbling rales, called mucous rales, are produced in the large bronchi or in those that have become dilated. The small moist rale, the subcrepitant rale, arises in the smaller tubes. The fine soft rale is produced in the capillary bronchi and indicates the presence of liquid exudate in them. The small moist rales are heard both in inspiration and expiration, and are thus differentiated from the fine inspiratory crepitation produced in the infundibulæ in pneumonia. In practice, however, this differentiation is in many cases impossible, as the small bubbling rale merges so imperceptibly into the fine crepitation that it is not possible to say where the one ends and the other begins. The large moist rales are found in the back and lower parts of the chest, as the secretions are carried to these parts by gravity. The moist rales of the bronchitis of tuberculosis are an exception to this rule; moist rales heard only at the apex of the lung are rarely other than tuberculous. Influenza, however, occasionally gives rise to circumscribed areas of bronchitis even in the apices.

An appreciation of the characters of rales is important in enabling us to determine the size of the bronchi affected, as the great danger in all cases of bronchitis is the extension of the inflammation to the capillary bronchi. A valuable sign of the involvement of the small bronchi was taught by Graves, viz., the persistence of a great number of rales audible over a small space, as a multiplicity of rales cannot be produced in the large bronchi, nor are they persistent.

**Clinical Forms of Bronchitis.**—Many classifications have been made on various bases, but the disease is so varied in its manifestations that none of them meets the needs satisfactorily. On an anatomical basis the disease is classified according to the size of the tubes affected, and some have adopted this in describing the disease, without reference to its cause, character, or duration. A second classification is clinical, and based on the severity and duration of the attack, as acute and chronic bronchitis, but the distinction between the two is arbitrary, as there is no definite time at which the acute merges into the chronic.

Marfan's classification on a bacteriological basis has already been given. Its adoption will necessitate as careful laboratory examination of the sputum as is now made in pneumonia. It will be found to be invaluable in many forms of bronchitis in determining early the prognosis and guiding the treatment, especially in influenza and streptococcus infections. But it will not be found quite efficient as a working basis, as the infection in most cases is too mixed to permit of the precise cause being determined; besides,

account will require to be taken of the part of the bronchial tree affected and of the duration of attack. Apart from the bacteriology, no advance has been made on the classification made by Walsh in his *Practical Treatise on the Diseases of the Lungs*, as follows: (1) Acute bronchitis (*a*) of the primary and secondary, (*b*) of all the bronchi, including the capillary. (2) Chronic bronchitis. (3) Special varieties: (*a*) fibrinous; (*b*) mechanical (scissors-grinders' and coal-workers'); (*c*) stone asthma; (*d*) acute specific forms (typhoid, syphilitic); (*e*) diathetic forms; (*f*) secondary forms in thoracic diseases.

Fowler simplifies this somewhat under the following headings: (1) Acute bronchitis (*a*) of the larger tubes; (*b*) of the smaller tubes. (2) Chronic bronchitis. (3) Secondary bronchitis. (4) Plastic bronchitis.

This combines in a measure the anatomical, clinical, and pathological classifications; and, in combination with the bacteriological one, affords a convenient working basis.

1. **Acute Bronchitis of the Larger Tubes.**—This variety is extremely common. It is often preceded by a coryza and begins with slight chilly sensations and feverishness. The severity of onset is usually in keeping with that of the subsequent course. In mild cases it may be limited to the trachea and larger tubes. There is some hoarseness, irritation in the throat, and not rarely a feeling of rawness behind the sternum. If the inflammation early affects the medium-sized tubes there is a feeling of constriction in the chest. Sleep is disturbed, the head aches, and there is a tired, bruised feeling of the body generally. Cough begins early, is at first slight and dry, but soon grows in severity, especially if the bifurcation of the trachea is affected; it increases the soreness beneath the sternum. There is marked lassitude, the expression is dull, and the eyes reddened. The tongue is heavily furred, the bowels constipated, and the urine scanty and high-colored. Thirst and loss of appetite are frequent. The pulse and temperature are only slightly affected. By the third or fourth day the cough becomes easier and less painful, and some semitransparent mucous sputum, containing many air bubbles and often streaked with blood, is brought up. It increases in quantity and soon becomes yellowish and opaque, losing its air bubbles. Coincident with this, the cough becomes easier and less paroxysmal. On auscultation, as a rule, no rales are heard, as the process is confined to the trachea and largest bronchi.

It may be remarked that paroxysms of coughing usually occur only in nervous people, and in the majority of cases the cough can be much controlled by a strong effort of the will. After two or three days, rapid improvement generally sets in, the tongue becomes clean, the appetite returns, and the patient feels better. Large and small mucous rales may be present; the cough becomes easy and there is free expectoration of opaque mucus containing yellowish or greenish streaks and spots.

In ten days or two weeks the symptoms will probably have disappeared with the exception of a slight tendency to cough on exposure to change of temperature, especially if the air is moist. After complete recovery the patient is apt to show a decided susceptibility to slight chilling with recurrence of bronchial symptoms. There is probably persistence in slight degree of the catarrhal condition of the trachea and larger bronchi, because it may be many months before the normal resistance is restored. It is in such cases that we meet with the so-called *winter cough.*

A first attack of bronchitis may develop suddenly in a person who has been quite well, but in the majority of cases there is a history of slight cough from time to time following exposure to cold or draught; no doubt some tracheitis has existed in such cases.

Adults are the most frequent sufferers from bronchitis of the larger and medium-sized tubes, but it is not rare in children and in them the symptoms are usually more severe. In children, in whom the equilibrium of the nerve centres is unstable, the attack may be ushered in by a convulsion. The temperature may be high, 104° or more, but it is usually quite irregular and falls rapidly. The pulse and respiration are relatively higher than the temperature. Delirium is frequent in the severer cases. The cough is paroxysmal and severe, the sputum being swallowed. Dyspnœa may be quite marked, the respiration being as high as 40 or more to the minute. In adults, at rest, the breathing is quiet, but after paroxysms of coughing, exertion, or much talking, the respiration is quickened. There is more liability of extension of the inflammation to the small tubes in children than in adults.

**Diagnosis.**—In the adult the diagnosis is seldom difficult or uncertain, yet cases are met with that baffle the most skilful. The difficulty is not so much in diagnosing bronchitis as in being certain that it is the primary and only affection, and not secondary to some other disease whose symptoms are latent or masked, as whooping-cough, influenza, typhoid fever, or acute tuberculosis. Much can be done to prevent error by careful bacteriological examination of the sputum. However, even the finding of pneumococci, streptococci, or influenza bacilli in the sputum does not necessarily exclude the existence of some latent disease, although it will furnish strong grounds for such exclusion.

A localized bronchitis is usually symptomatic; for example, bronchitis limited to the apex may be the first sign of pulmonary tuberculosis, that of both bases is usually due to hypostatic congestion, resulting from cardiac disease. Influenza also often causes localized bronchitis. Bronchitis of the larger tubes, especially in children, may be due to irritation from enlarged bronchial glands; in such cases the cough is generally of a violent, convulsive character. A similar cough may be caused by disease of the upper air passages, and by foreign bodies in the bronchi. In mitral stenosis the bronchi are very susceptible to catarrhal infection; in such cases the sputum may contain some bright-red blood, often in large quantities, and the affection may be confounded with tuberculous disease.

*Incipient pulmonary tuberculosis* may simulate simple bronchitis. There is usually a history of gradual failure of health, yet it must not be overlooked that tuberculosis is not rare in stout, florid people, who are apparently in good health and complain of nothing but an irritating cough with scanty expectoration. No signs may be found on examination, or, at most, only a few evanescent, moist, or piping rales at one apex. A hasty diagnosis should not be made in such a case, as unnecessary anxiety may be excited and undue therapeutic measures undertaken. Careful observation is necessary, and if still in doubt a tuberculin test should be made.

Miliary tuberculosis is generally marked by a higher and more persistent fever, more prostration, and greater shortness of breath. It will not be amiss to repeat that the fullest investigation of the sputum, when present, affords, with few exceptions, the most certain basis for a diagnosis.

**Prognosis.**—Except in the very young and in the aged, the bronchitis of the larger tubes is rarely fatal, but there is considerable uncertainty as to the duration of the attack and the completeness of recovery. By the profession as well as the public the affection is viewed with too much indifference, and to the want of care is often due the frequency with which slight catarrhal affections of the trachea and larger bronchi persist after acute bronchitis. Mild cases usually require ten days or two weeks, and severe ones, especially the streptococcus cases, three or four weeks to make a satisfactory recovery. Even after that, the recovery in many of them is incomplete and they are susceptible to recurrences of cough after slight chills. In the emphysematous, recovery is nearly always tedious, often requiring several months, especially in cold, damp climates.

A fatal termination scarcely ever occurs, except in young children and old people, or in patients suffering from such grave diseases as nephritis, heart disease, diabetes, chronic bronchitis, and emphysema; in these bronchopneumonia is a frequent and dangerous sequel. The signs of danger are the evidences that indicate failure of the right ventricle, as cyanosis, pulsation in the veins of the neck, visible cardiac impulse at the lower end of the sternum, great dyspnœa, short ineffective cough, cold sweat, and a weak, rapid, irregular pulse. There is little hope of recovery in a case presenting such a symptom-group.

2. **Acute Bronchitis of the Smaller Tubes, Capillary Bronchitis, Suffocative Catarrh.**—The division of bronchitis into (1) that of the larger tubes and (2) that of the smaller tubes is made purely for clinical convenience. It has no anatomical basis, as there is no anatomical distinction between the two. Then again the lower limit of bronchitis of the larger tubes is not definite; in mild cases the inflammation may be confined to the trachea and largest bronchi, while in severe ones the inflammation probably spreads in many parts of the lungs down to quite small bronchi, yet, as the breathing surface is unaffected, and with the great breathing capacity of a vigorous adult, the respiration is not materially disturbed.

Bronchitis of the smaller tubes is of much more frequent occurrence in children, in whom also it causes much graver symptoms, as the bronchi readily become obstructed. This is due to two causes: (1) The small size and incomplete rigidity of the tubes as compared with those of the adult, so that a small amount of secretion may produce a large degree of obstruction. (2) The difficulty which children experience in expelling the secretion from the tubes. This is owing (*a*) to their smaller chest capacity, *i. e.*, to the smaller volume of air which can be used to force the obstruction out; (*b*) to their feeble muscular power; (*c*) to the want of rigidity in the thorax, and (*d*) to their ignorance of the proper method of coughing; for coughing, which is effective in dislodging an obstruction from the air passages, is a habit unconsciously developed in the adult wholly by practice, and little children have not had time to acquire it.

Many writers believe that in all cases of capillary bronchitis there is extension of the inflammation to the lobules of the lung, and that the disease is therefore a bronchopneumonia and should be considered as such. The difference of opinion is due to the want of precision in the use of the term capillary bronchitis. If it is held to mean inflammation of the terminal bronchi that open into the infundibular spaces, then in all cases the implication of the lung is inevitable; but if inflammation of the small tubes

above the terminal ones is implied by the term, there is no doubt that the disease may and does often occur without implication of the pulmonary lobules, although the liability to such implication is very great.

**Etiology.**—Capillary bronchitis is especially liable to occur in the following diseases in the order of sequence: measles, whooping-cough, influenza, and typhoid fever. In pulmonary tuberculosis, capillary bronchitis due to the pneumococcus may develop and be rapidly fatal from asphyxia. Certain conditions favor the extension of catarrh to the small bronchi: (*a*) Children in the first five years are very susceptible. Their failure to expectorate favors the extension of the process to the small bronchi by inspiration of secretion. Rickets by deforming the chest also increases the liability. (*b*) The aged are also frequently affected, owing to vascular changes, defective expectoration, debility, and frequent prolonged dorsal decubitus. (*c*) All cachectic states, especially if associated with prolonged dorsal decubitus, are also favoring causes. The exciting cause does not differ from that of disease of the larger tubes; both forms are essentially infectious, streptococci and pneumococci being the most frequent microörganisms. The influenza bacillus is probably the cause in many cases.

**Special Pathology.**—The lungs may be distended with air and in parts markedly emphysematous. Areas of collapse, smaller or larger, even of a whole lobe, may be present. On section small drops of pus may be expressed from the bronchioles. The small size of the bronchi, the intensity of the inflammatory process, and the free exudation account for the rapid obstruction of the capillary bronchi; the mechanical effect on the lung results in atelectasis and emphysema.

In atelectasis the affected parts are seen as flat or depressed areas, violaceous in color, non-crepitant, and heavier than water. The areas can be restored to a normal state by inflation. They are found chiefly in the periphery of the lung.

Three theories have been advanced to account for the occurrence of atelectasis: (1) Gairdner explained it by the ball-valve action of the mucus filling the small bronchi; in expiration the ball of mucus is carried out toward a larger bronchiole, allowing the air to escape, but with inspiration it is forced back, effectually preventing the entrance of air into the alveolus, which soon becomes empty and collapses. (2) Virchow, Ziemssen, and others attribute the collapse to absorption of the contained air, the entrance of more being prevented by the obstruction from stationary secretion. (3) Charcot and his pupils believed the condition to be a true broncho-pneumonia.

*Vesicular emphysema* is frequent in suffocative catarrh; it occurs in the upper anterior parts of the lungs and is due to the loss of elasticity of the lung due to cough and dyspnœa.

The lymph glands at the root of the lung are always somewhat inflamed. The liver is large, and presents areas of fatty degeneration which have been attributed to the toxin of streptococci. The spleen is enlarged and shows the appearances usually found in infectious diseases.

**Symptoms.**—There is a division of opinion as to whether capillary bronchitis begins primarily as such, or is secondary to a catarrh spreading downward from the larger tubes. It is probably more often primary. Clinically it is characterized by the intensity of the symptoms of toxæmia and asphyxia and the suddenness of its evolution. In children the onset is

usually sudden, not rarely with a convulsion. The temperature rises rapidly, it may be to 103° or 104°, with a hot, dry skin, and restlessness. The cough is short, frequent, and dry; it may be paroxysmal. Respiration becomes rapidly increased in frequency, and may rise to 60 or more in the minute. Each respiratory act is short and quick, the inspiration energetic, and expiration difficult and requiring the aid of the accessory muscles. The pause after inspiration is often longer than that after expiration. The face is anxious, the lips and cheeks soon show cyanosis, and the alæ nasi are widely dilated and dilate and contract in each respiratory act. Frequent attacks of coughing distress the child, but bring no relief. As the difficulty of breathing increases, the restlessness becomes more marked; the child sits up in bed, draws up his knees, soon lies down again, then wishes to be taken into the nurse's arms, but soon returns to bed. As the cyanosis deepens, he gradually becomes quieter, often with some mild delirium. The skin is usually dry and hot, and the thirst great.

The *physical signs* do not differ greatly from those of the disease in the larger tubes. The upper part of the chest is distended while the lower is retracted. The percussion note rarely shows distinct changes; areas of dulness are difficult to demonstrate, as they are often surrounded by zones of distended lobules that obscure the dull note. Large areas of atelectasis may give faint temporary dulness, which disappears with the expansion of the collapsed lobules. If these areas become pneumonic, the dulness, of course, persists and usually extends, but even well-marked patches of pneumonic consolidation are often revealed by autopsy when only suspected during life. On auscultation, the respiratory sounds vary; they are loud and harsh over the parts of the lungs that are little altered; weak over emphysematous parts, and also at the bases, where collapse of vesicles is most frequent and the tubes are occluded by secretion. The rales are small and bubbling, simulating crepitant rales. Rhonchial and sibilant sounds, especially the latter, may be present, chiefly in the upper and front part of the chest. The abundance of diverse rales is remarkable. They are persistent and unaltered by coughing (Graves' sign). The pulse becomes very rapid, ranging from 120 to 160 or more; it is small, dicrotic, and difficult to count.

As the general prostration increases the delirium may become continuous; there may be clenching of the fingers over the thumb flexed into the palm, which is a common and early symptom, and later becomes very marked; and the pulse and respiration increase in rapidity, being much more disturbed than the temperature. Coma usually deepens gradually and convulsions may close the scene.

In less severe cases the stupor may end in a sleep from which the child awakens improved; the breathing is easier, the cough looser and sputum raised more freely; the pulse grows slower and stronger, and cyanosis gradually fades, but the danger is not yet past, as there may be a recurrence of the catarrhal process with a fatal ending.

**Diagnosis.**—The diagnosis of this form of bronchitis is often very difficult. The dyspnœa, the auscultatory signs, the fever, and the signs of intoxication and asphyxia distinguish it from ordinary bronchitis. Graves' sign is also distinctive. As already pointed out, there are many who think that the lungs are affected in all cases and that the condition should, therefore, be regarded as bronchopneumonia. In the severe cases it is not possible to

differentiate the two diseases with certainty; in such cases the lung if not affected becomes so very soon. However, when only the smaller tubes are affected the onset of the attack is less marked; chill and convulsion are less frequent, and the temperature is less disturbed. The physical signs, if distinct, afford the only certain ground for a diagnosis, the presence of bronchitic rales in all parts of both lungs, and the absence of signs of consolidation excluding pneumonia.

In emphysematous cases, however, pneumonia may occur in small areas without any evidence of consolidation. Yet in some of these the diagnosis of pneumonia is rendered possible by the occurrence of distinct tubular breathing.

Unfortunately, examination of the sputum, when it can be obtained, does not aid in distinguishing bronchopneumonia, as both diseases are caused by the same varieties of bacteria. Miliary tuberculosis and acute pneumonic phthisis would be shown to be present if bacilli were found, but these diseases simulate bronchopneumonia rather than capillary bronchitis.

Asthma, especially a first attack, may usually be differentiated by the sudden onset and the absence of fever and of the severe cough. In some cases of acute bronchitis there are symptoms of marked bronchial spasm which may occasion doubt for a time.

**Prognosis.**—A severe attack of bronchitis in an infant may be fatal in a day; if less severe it may drag on for a week or more before death. In older children the duration is longer and the recoveries more frequent. The healthy adult is rarely affected, but in the feeble, especially in those whose circulation is weakened, the disease is not rare, and may be fatal in a few days. The unfavorable signs are those that point to failing power in the respiratory, circulatory, and nervous systems, as dyspnœa, lessening in frequency and force of cough, and consequent cessation of expectoration, cyanosis, delirium, coma, and convulsions.

**Capillary Bronchitis in the Aged.**—Bronchitis is one of the commonest affections of old people and shows a remarkable tendency to extend to the smaller tubes. The affection in the aged and in children constitutes the condition designated by Sydenham "Peripneumonia Notha." The tendency to great exhaustion is the most characteristic feature of the disease in the aged; in other respects the symptoms do not indicate the gravity of the affection. There is usually no fever, the pulse is good, and the respiration only moderately quickened. Expectoration is easy as a rule, and the cough, therefore, not excessive. But there is a marked tendency to depression and drowsiness. The nights are restless, appetite is lost, but thirst is usually marked; hence the urine is copious and in the drowsy state is frequently passed unconsciously. The disease is most frequently due to a streptococcus infection, and if not early fatal generally passes into a chronic bronchitis.

Most cases terminate finally in bronchopneumonia, but this develops so insidiously, as a rule, that it may escape detection even by the most acute observer. Cough and expectoration often diminish, the temperature and respiration remain undisturbed, but the pulse grows weaker and more rapid as the vital powers fail. Physical examination may reveal evidences of local consolidations, but in many cases there are no signs to be found. In fact, in many old people who have shown no symptoms but prostration with somnolency and feeble pulse, the morbid changes of unsuspected bronchopneumonia are found at the autopsy.

**Prophylaxis.**—Much can be done to prevent catarrhal affections by the adoption of a healthful manner of living. Next to good, well-prepared food cleanliness is of the first consideration, cleanliness of air, as well as of person and surroundings. Air not being tangible, its purity does not appeal to the masses as do other forms of cleanliness. In the crusade against tuberculosis the necessity of fresh air has been so much insisted on that its importance in the maintenance of health, as well as in the treatment of other diseases, is in danger of being lost sight of. Next to a vigorous, outdoor life should be placed the daily cool bath, the temperature being graded according to the age and constitution of the individual. The clothing, the bed, the sleeping-room, the avoidance of chill in dressing, and many apparently trivial matters should receive careful attention. All these considerations require attention, not only to keep the healthy well, but also to increase the resistance to recurrences of the attacks in those who have had bronchitis. Unhealthful occupations, especially those in which there is much dust and the air is impure, should be avoided. The dwelling-rooms should not be overheated, nor the air too dry. The clothing should be light, absorbent, and suitable for the season, but burdening with clothes in any season should be avoided. Coddling, as well as irrational exposure, like all extremes, is bad. In all cases the nasopharynx should receive appropriate treatment, if catarrhal processes or chronic thickening of the lining membrane be present, as this is so frequently the source of infection of the bronchi.

**Treatment.**—In the opinion of most people mild cases of bronchitis do not require any treatment, as they deem it but a slight ailment. They therefore seldom stop work or modify the routine of the daily life, too often with serious consequences.

As the affection is common and there is no specific treatment, it follows that many plans of treatment have been tried, rational and irrational. As in other diseases, so here, the patient rather than the disease should be the object of treatment. As patients differ so much in vigor and constitution, it is not surprising that various and even opposite plans of management should often prove equally successful in attaining the object aimed at. No uniform course of treatment can be the best for all, so that each case should be considered on its own merits. Our aim is to secure arrest of the affection and the removal of its effects in the shortest possible time.

*Rest* is of the first importance; all patients recover more quickly if kept to their rooms, and in well-marked cases the patient should be kept in bed during the acute stage. The clothing should be sufficient for warmth, but not burdensome. The temperature of the room is usually most agreeable at about 70°, as least likely to excite cough. The air should be pure and contain a moderate amount of moisture. Of late years a large and growing number of capable observers have advocated the free admission of cold, pure air to the patient with serious bronchitis or bronchopneumonia. Cold air is more dense than warm air, and therefore contains more oxygen per volume; it also stimulates respiration so that the inspirations are deeper and the blood therefore becomes better aërated. Cold air, however, especially if moist, may excite cough and dyspnœa, probably by causing spasm of the bronchi; in such cases the admission of cold air is not desirable until the excessive irritability has been relieved. Long confinement to warm rooms is injudicious in all cases; if protection from cold and moisture is necessary a mild, dry climate should be sought.

As regards applications to the chest, the extremes of heat and cold, with all variations between, are used. The object of all of them is to lessen hyperæmia and swelling of the bronchial mucous membrane, and thus remove or reduce the obstruction to the entrance of air. As none of these applications can have any direct influence on the vessels of the mucous membrane their influence must be reflex. It is known that cold applied to the surface causes blanching of the bronchial mucous membrane; but if the cold is continued too long the membrane soon becomes congested again. Heat possibly acts in a similar manner, although it may be that the action of both is due in part to the fact that they allay spasm of the bronchi. Both heat and cold often give effective relief, but cold has the advantage in that it is more easily applied, and that it excites deeper inspiration. Cold is most easily applied by using a *compress* of two to four layers of gauze, old linen or cotton, cut large enough to cover the whole chest; the compress is wrung out of cold water, applied closely so as to be in intimate contact with the surface of the chest and covered with a dry, thin flannel, to permit of evaporation. The coldness of the water and the frequency of changing the compress must be regulated according to the patient's strength and the urgency of the symptoms.

*Cold affusion* is also a simple method of applying cold to the surface; it should be applied while the patient stands in warm water. This method is especially convenient and therefore most applicable to the treatment of capillary bronchitis of children. The *cold wet pack* is very useful for nervous patients. Cold douches and cold rubs are more stimulating and are therefore suitable for the vigorous. *Vapor baths* or *Turkish baths* in the early stage of acute bronchitis do much good, especially if the perspiration be free.

*Warm baths* of long duration are the best form for chronic bronchitis.

Heat is usually applied by a poultice of linseed meal, with or without mustard. The poultice, to be effective, must be applied very hot, burning being prevented by a layer or two of flannel placed beneath it, and the whole covered with flannel, wax paper, or rubber cloth to retain the heat as long as possible, and hold the poultice in close contact with the chest. The whole front of the chest should be covered with the poultice, which should be changed on cooling. It is difficult to accurately estimate the value of poulticing, but that the benefit derived from its use is much less than is generally supposed by the profession and public there is no doubt. Chief among the objections to its use is the great weight, a grave fault, as in serious cases the muscles of respiration are already overtaxed, and it is in these that the poultice is most needed. The use of a poultice or even a so-called "pneumonia jacket" on the chest of a child, whose respiratory muscles are already taxed in maintaining the breathing, is certainly not rational therapeutics. It has, however, often to be used out of deference to public opinion.

Free perspiration, especially at the beginning, often moderates and not rarely aborts an attack. A full warm bath, at a temperature of 100° to 105°, for ten to fifteen minutes is usually effective. The patient should be at once placed in a warm bed, and diaphoresis encouraged by giving hot drinks. Hot bottles may be put around the patient, who is covered by blankets.

*Inhalations.*—These are probably next in importance, especially in acute cases. Even the vapor from hot water is grateful and soothing to the irritable bronchial mucous membrane. Its efficiency can be increased by adding various volatile and antiseptic remedies, either sedative or stimulant, such as

eucalyptol, thymol, oleum pini sylvestris, or compound tincture of benzoin, of any one of which about a drachm is to be put into a pint of water at 150°. A dram or more of light carbonate of magnesia is usually added. Camphor, of which menthol is most commonly used, is an excellent addition, about 2 grains being added to a pint. Carbolic acid is also useful. Several ingredients may be effectively combined, as follows: Oleum pini sylvestris, oil of eucalyptus, of each 15 grains (1 gm.); menthol, 5 grains (0.3 gm.); light carbonate of magnesia, 10 grains (0.7 gm.); compound tincture of benzoin, 1 oz. (30 cc.). Of this combination a teaspoonful is to be put into a pint of hot water and the vapor inhaled.

Atomizers and nebulizers are useful, chiefly for the application of spray to the upper air passages, although after their use tests have shown the presence of the medicine in the pulmonary alveoli and in cavities. Simple saline solutions are much used; they quiet the cough and render secretion more liquid. They have more effect in the early stages. In severe cases they should be used frequently, every two or three hours for a few minutes at a time. After the acute stage is passed, the addition of such an antiseptic astringent as sulphocarbolate of zinc, 1 or 2 grains (0.07 or 0.13 gm.) to the ounce, is useful when the trachea and larger bronchi are affected.

*Internal Remedies.*—In simple colds, confinement to the room, a little opiate, and a hot drink usually suffice to give relief. In more severe forms with fever and aching pains, *quinine sulphate*, 7 to 10 grains (0.50 to 0.75 gm.) per day, if given at the beginning of the affection and during the following three or four days, may quickly cut short the general symptoms and lessen the duration. If quinine fails to give relief, antipyrine or phenacetin may be tried; they usually relieve the general symptoms.

In the early stage of the disease the vascular depressants are much used, as they cause the vessels to dilate and thus increase the secretion, especially the serous portion of it. They are the so-called sedative expectorants, such as tartarated antimony, ipecacuanha, apomorphine, and pilocarpine. Of these, pilocarpine is the most effective; apomorphine is next, but is used more often; opium may be added to this group, but it is, as a rule, given to allay cough by diminishing the irritability of the mucous membrane. The dose of these depressants should be small and frequently repeated to maintain their effect. Of pilocarpine, from gr. $\frac{1}{125}$ to $\frac{1}{60}$ (0.0005 to 0.001 gm.) three to four times a day should be sufficient for an adult; West gives gr. $\frac{1}{8}$ (0.008 gm.) three times a day. Apomorphine, gr. $\frac{1}{10}$ (0.006 gm.), gradually increased to gr. $\frac{1}{5}$ (0.013 gm.), will usually cause copious bronchial secretion. If given early, tincture of aconite, ♏j (0.06 cc.) every fifteen or twenty minutes for about eight doses, will generally cause free perspiration and a fall in the temperature. It is quite safe for persons of ordinarily robust health. The addition to any of these drugs of liquor ammonii acetatis, ʒiij to iv (12 to 16 cc.), and spirit of nitrous ether, ʒss to j (2 to 4 cc.), increases their efficacy by stimulating diaphoresis. These remedies are being used with less and less frequency, as they are more or less nauseating; hot teas and salines usually answer the purpose for which they are given equally as well. They are only of use while the secretion is tenacious and scanty, and they should not be continued longer than a few days.

The rational use of opium in cough should be clearly understood. Useful cough, that is, cough which is required to keep the bronchial secretion moving outward and prevent its accumulation, is necessary for the safety of the

patient, and should not be quieted by opiates. On the other hand, useless cough, that is, cough not due to accumulating secretion, and cough in excess of what is required to prevent accumulation of secretion, is fatiguing and tends to exhaustion, and should therefore be controlled. In affections of the smaller bronchi frequent cough is necessary to prevent obstruction, especially in children, as their chest walls are so elastic as to render effective coughing difficult, even impossible, if much secretion has accumulated. In the aged the irritability of the respiratory centres is so low that a little opium suffices to make them quite insensible to the presence of the bronchial secretion. Therefore, in both classes opiates are dangerous remedies; yet in both if given guardedly, they may do much good and be indispensable, at least in the aged, in whom opium is often the most powerful restorer of vitality.

Small doses of morphine, gr. $\frac{1}{60}$ to $\frac{1}{50}$ (0.001 to 0.0013 gm.), may, in the aged, suffice to relieve the excess of cough and at the same time improve the general condition; the utmost caution is, however, necessary to obviate such depression of the sensory centres as to lead to retention of secretion in the bronchi. The derivatives of morphine, especially heroine, gr. $\frac{1}{80}$ to $\frac{1}{16}$ (0.002 to 0.004 gm.), and codeine, gr. $\frac{1}{8}$ to $\frac{1}{4}$ (0.008 to 0.016 gm.), may prove quite as effective and be less likely to cause undue depression. The danger of opiates is especially great when the smaller bronchi are extensively affected, as then frequent cough is necessary to prevent obstruction. The labored breathing, the frequent cough, and the excess of carbonic acid in the blood produce such a sense of great fatigue and desire to sleep that a sedative to give sleep is often begged for; to yield to the solicitation would be to take away the last chance of recovery. If the dyspnœa is less urgent, one or two hours' sleep may be induced by one of the bromides, gr. 10 to 15 (0.7 to 1 gm.), with a small dose of chloral, gr. 5 to 10 (0.3 to 0.7 gm.); but the sleep should be short, and coughing and expectoration encouraged when the patient awakens.

If the cough becomes ineffective and mucus accumulates to such an extent that suffocation threatens, an emetic must be given, such as gr. 20 (1.3 gm.) of ipecacuanha. Apomorphine is more rapid and certain and rarely causes depression. A dose of gr. $\frac{1}{8}$ (0.013 gm.) by the mouth or gr. $\frac{1}{10}$ (0.007 gm.) subcutaneously usually suffices in the adult; for young children, about gr. $\frac{1}{25}$ (0.0027 gm.). The act of vomiting usually forces much of the mucus out of the bronchi with great relief to the breathing.

*Bleeding* was once regularly resorted to in bronchitis as in other inflammatory diseases, but its indiscriminate use doing much damage, it fell into disrepute. Of late the practice has been somewhat revived, and with gratifying results when judiciously used. "It does most good in robust, full-blooded adults in acute attacks" (West), but bronchitis in such patients rarely needs such heroic measures. It is with signs of overstrain of the right ventricle, such as dyspnœa, commencing cyanosis, rising pulse, etc., that bleeding is called for. It produces gratifying results if it lessens the distention of the right ventricle so as to enable it to contract fully and raise the pressure so as to force the blood through the pulmonary capillaries. To be effective the bleeding should be free, as the relief of the distention of the right ventricle depends on the suddenness with which the volume of blood flowing to it is reduced. Children, the aged, and the very feeble of all ages do not bear bleeding well; the advisability of resorting to it in others is

to be estimated by the state of the right ventricle. Ten to fifteen or twenty ounces should be removed; saline solution can be given subcutaneously after the heart has been relieved, if the loss of blood is considered a serious matter for the patient.

Purgatives are permissble in all cases, and their free use somewhat relieves engorgement of the right heart by reducing portal congestion. Those producing copious liquid stools are the most effective. Care should be taken to prevent flatulence, as distention of either stomach or bowel interferes with the action of the diaphragm, and therefore lessens the respiratory capacity.

Whether practical benefit results from the inhalation of oxygen in severe bronchitis is doubtful. That it should be of benefit seems most reasonable; but it often fails to do good, and may even add to the patient's distress by proving irksome to him. If its administration is begun before severe dyspnœa has set in, while the patient can still with ease inhale the gas, it is probable that he will be able to continue its use at a later stage, when the breathing has become much more distressed; given in this manner oxygen may prevent the development of the graver symptoms.

The hypodermic injection of strychine is recommended as a stimulant to the respiration and circulation, as it increases the irritability of the nerve centres. It should increase the cough and the depth of inspiration, and be therefore an aid to the other means of treatment.

If the heart shows signs of failure, caffeine may prove an efficient cardiac stimulant. The pure alkaloid is the most reliable; gr. 3 to 5 or more (0.2 to 0.4 gm.), rendered soluble by the addition of benzoate or salicylate of sodium, may be given hypodermically every three hours. Digitaline may be added.

Alcohol, especially in old people, may do much good in quieting restlessness and calming a weak, irritable heart. Six or seven ounces of brandy or whisky may be required in the twenty-four hours. But it is to be borne in mind that it is only to the exceptional cases that it should be given, and not to all; nor even to any as a matter of routine.

The nursing of bronchitis is of great importance, especially in severe cases, as relapses are very liable to occur. The patient should be carefully guarded against chilling, a danger liable to occur if the temperature of the room is permitted to fall or the air to become impure. The more severe the attack, the more frequently should the patient be awakened at night so that cough may be excited to ensure the expulsion of secretion and prevent dangerous accumulation in the bronchi.

The drinking of liquids freely is desirable, in order, by stimulating the action of the skin and kidneys, first, to reduce reflexly the congestion of the bronchial mucous membrane, and, secondly, to remove toxic substances which might act as irritants. If there is no appetite, liquid food may be given and a gradual return made to a solid diet. Care should, however, be taken to prevent distention of the stomach by either gas or liquids. In the young, the aged, and the feeble, extreme care is needed to maintain strength and yet not overtax the powers of digestion. Liquid foods are usually all they can digest. The diet should be regulated according to the patient's appetite and digestion. In adults of ordinary vigor, if there is no desire for food, none is required for the first day or two.

*Summary.*—It may prove useful to conclude with a summary of the treatment of acute bronchitis. In the adult at the beginning of an attack

diaphoresis should be induced by a hot bath and hot drinks taken at bedtime. A tablespoonful of liquor ammonii acetatis, with a teaspoonful of spirit of nitrous ether, every hour or two, will aid in stimulating diaphoresis. In the more robust, a Turkish bath, if taken early, may be effective in aborting an attack, but the patient should be at once put to bed, as returning home even in a warm, closed carriage is unwise. If necessary, pilocarpine, gr. $\frac{1}{20}$ to $\frac{1}{10}$ (0.003 to 0.006 gm.), may be given to cause perspiration and free secretion from the mucous membranes. A cold compress to the throat and chest should be applied at night, to be changed every two hours in severe cases. If preferred, hot compresses or poultices, with or without the addition of mustard or hot liniments, may be applied. In any case, the body and limbs should be kept warm. Inhalations of warm saline solution in fine spray at short intervals do much to soothe irritability, lessen congestion, and promote secretion and disinfection. The bowels should be freely opened by a saline, or a hydragogue cathartic. The air should be warm, fresh, and moist. If cough is troublesome, vapor of hot water to which is added such a mixture as the following will be useful:

| | | |
|---|---|---|
| Olei pini sylvestris, | | |
| Olei eucalypti | āā | ℥ss (2 cc.). |
| Creosoti | | ♏ x (0.6 cc.). |
| Menthol | | gr. x (0.6 gm.). |
| Tincturæ benzoini compositæ | | ℥ij (60 cc.). |

A teaspoonful in a pint of hot water is used as an inhalation or, by adding glycerin ℥ij, it may be used in a nebulizer.

If it seem undesirable to give pilocarpine, and the cough is dry, wine of antimony or Brown mixture (mistura glycyrrhizæ comp., U. S. P.) may be substituted, as in the following, to be taken every three hours:

| | | |
|---|---|---|
| Vini antimonialis, | | |
| Vini ipecacuanhæ | āā | ♏ x (0.6 cc.). |
| Misturæ glycyrrhizæ compositæ | | ℥j (4 cc.). |
| Liquor ammonii acetatis | q. s. ad | ℥ss (16 cc.). |

If the cough is harassing, heroine, gr. $\frac{1}{80}$ to $\frac{1}{16}$ (0.002 to 0.004 gm.), may be added to each dose, or codeine, gr. $\frac{1}{8}$ to $\frac{1}{4}$ (0.0075 to 0.015 gm.). Dover's powder is an old and useful remedy in doses of 5 to 7 grains (0.3 to 0.5 gm.).

In the next stage, when the cough, although frequent, is not more than is required for expectoration, terpene hydrate and ammonium chloride, 5 grains (0.35 gm.) each in capsule every three hours, may be of use. If the cough is excessive, one of the sedatives noted above may be added.

The general condition should be carefully scrutinized, and suitable treatment for it carried out. Change of scene is the best restorative that can be prescribed for most patients, especially from cold, wet climates to warm, dry ones, where an outdoor life can be led. Iron, strychnine, cod-liver oil, quinine, and arsenic should be given as indicated by the general condition. Cardiac stimulants will be needed in those suffering from defective circulation. In those in whom cough persists, careful examination of the upper air passages should be made, as local patches of inflammation may be found in the trachea or larynx, or even in the nose and pharynx, to which the cough and expectoration are due and for which local treatment is required.

In the aged and feeble, depressing remedies should not be given; such require stimulation with wine, spirits of ammonia, digitalis, strychnine, etc.

In young children, expectorants and opiates are rarely admissible; if given, it must be with the greatest circumspection. Cool compresses are useful and easily applied; if preferred, hot ones may be used instead, but poultices are objectionable on account of their weight and the difficulty of applying them properly. Warm baths are easily given; a bath at 105° or even 110°, with four or five tablespoonfuls of mustard, forms an effective derivative, and a stimulant to respiration and circulation. Five to ten minutes are sufficiently long for the bath.

Inhalations are of great value. At first, vapor of plain water, or lime-water, is best; later, creosote, turpentine, camphor, or menthol may be added. The cot may be partially surrounded by a canopy, but it is of the greatest importance that the air be kept fresh. A large vessel of boiling water consumes no oxygen and is, therefore, better than heating a small vessel with a spirit lamp.

Except in conditions of great prostration, emetics should be given if the secretion is accumulating in the bronchi, the cough not being effective. They serve the double purpose of expelling the mucus from the bronchi and inflating collapsed pulmonary lobules by the deep inspiration that precedes the act of vomiting. Syrup of ipecac is an efficient emetic for such cases and does not depress. Rolleston has given many children apomorphine, gr. $\frac{1}{80}$ (0.002 gm.) hypodermically, with good effect, adding strychnine, gr. $\frac{1}{200}$ (0.0003 gm.), to counteract its depressing effect. In such a condition deep inspiration should be excited by alternate hot and cold douches, or by causing frequent crying by spanking, as recommended by Jacobi. Oxygen inhalations, to be useful, should be given early.

Cardiac and respiratory stimulants are required in all severe attacks. Alcohol is probably the best, and should be given as soon as signs of prostration are shown. Strychnine is the most effective respiratory stimulant; it increases the irritability of the respiratory centres and therefore increases the cough. Belladonna is highly commended by many as a respiratory stimulant. One minim (0.067 cc.) of the tincture may be given every two to four hours to an infant six months old. Its effects should be watched and the dose reduced when signs of improvement show themselves.

If there is cyanosis, dry cups applied between the shoulders and to the upper lumbar region may be of much benefit.

In emphysema and other conditions in which there is difficulty in expelling secretion, Ewart has found decided benefit from regularly compressing the sides of the chest during expiration, by the outspread hands applied over the axillary regions, the patient meanwhile lying prone with the head over the side of the bed. The benefit would be in proportion to the elasticity of the chest wall, and therefore not of much use in old people.

In all cases the patients should be kept in their rooms until all rales have disappeared and the cough is notably diminished if not completely arrested. In feeble old people, in cardiac disease, and in subjects with weak resistance to tuberculous infection there is a strong tendency for the bronchitis to persist or to become chronic; in such cases the application of counterirritants to the chest may hasten resolution of the bronchial inflammation.

**Chronic Bronchitis.—Etiology.**—Chronic bronchitis is a term of wide application, and embraces many conditions attended by long-continued inflammation of the bronchial mucous membrane. It may occur inde-

pendently or secondarily to some other disease, which it often obscures by the prominence of its symptoms. Chronic bronchitis does not require special causes for its production, but may originate from any of the causes referred to in the study of the general etiology, especially when their action is persistent or frequently repeated. Furthermore, defective qualities of the bronchial mucous membrane, natural or acquired, are of importance in some subjects.

1. It often follows *acute bronchitis*, and if the primary acute infection is intense, or has been often repeated, the mucous membrane is slow in returning to a normal state and is therefore less able to resist the invasions of bacteria. It is in this manner that the great majority of cases originate.

2. *Diseases of the nasopharynx* (chronic catarrh, adenoids, nasal obstruction, etc.) may cause it, partly by gradual extension of the affection to the trachea and bronchi, and partly by injury to the bronchial mucous membrane resulting from mouth breathing.

3. Many cases are secondary to *constitutional maladies*, such as gout, rickets, chronic nephritis, scrofula, etc.

4. *Conditions that disturb the circulation* so as to impede the flow of blood through the lungs are the cause in many cases; heart affections, especially incompetence of the mitral valves; chronic lung affections, such as emphysema and tuberculosis; enlarged bronchial glands; pleural adhesion and obesity. Alcoholism is an important cause; it acts partly by disturbing circulation and partly by increasing the toxic substances in the blood. Excessive smoking acts in a similar manner.

5. A fifth group of causes includes irritants in the atmosphere acting directly on the bronchial mucous membrane, such as dust, irritant gases, fumes from lime, etc.

6. Auto-intoxication from chronic dyspepsias, especially those in which there is *gastric dilatation*, has been assigned as a cause by Bouchard and his pupils.

As in acute bronchitis, so here all causes act by disturbing the circulation and nutrition of the mucous membrane, reducing its vitality so that microorganisms are able to excite inflammatory changes in it.

**Symptoms.**—In general, they are those of bronchitis without the acute symptoms; in fact, it is often difficult to differentiate between mild recurring attacks of acute bronchitis and the chronic variety. In many of these cases of recurring attacks, some inflammation persists between the attacks, in the trachea and larger bronchi, with, at most, only slight occasional cough and little expectoration, most frequently in the morning. Many of the cases of *winter cough*, the most common form of chronic bronchitis, have a history of preceding recurrent attacks of the acute disease, but many of them develop gradually and without acute symptoms. The trachea and large bronchi only are affected and therefore no physical signs are evident. People past middle life are most frequently affected, especially those who are rather stout and are given to free indulgence in food and drink. The bronchial affection begins as a troublesome morning cough which is often replaced by wheezing; the cough persists until the night's secretion has been expelled, after which there is usually relief for the remainder of the day. The recumbent position resumed at night may excite it again by the secretion falling to the posterior surface of the bronchi, which is the most sensitive part; as a rule, however, the night is undisturbed.

The sputum may be scanty, but it is often copious. It is muco-purulent, thick, and yellow, and may sink in water like that of chronic pulmonary tuberculosis.

If there is little or no emphysema, the breathing is normal; the general health is good and quite equal to the active duties of life. In a few years in most cases the relief in summer grows shorter and less complete and the cough in winter more severe, and the general health begins to fail. In time the symptoms persist throughout the year, although worse in winter, and as the smaller bronchi become affected and emphysema develops, dyspnœa becomes troublesome. The less severe cases may lead an active, useful life, and attain an old age.

When the disease is of a more severe type it affects the smaller tubes early; all the symptoms are more marked. The cough is more severe, may be paroxysmal and at times with more or less wheezing.

*Dyspnœa* in some degree is never absent; it is caused by the emphysema and interstitial pulmonary fibrosis which always develops. It becomes paroxysmal with an asthmatic type, if the secretion is abundant and adhesive so as to lodge in the tubes.

Slight causes are apt to excite exacerbations of cough, and necessitate confinement to the house or room for a few days. In the intervals, however, the general health is good. In more severe and advanced cases the symptoms are much worse. Cough is often most troublesome at night and expectoration may be profuse. There are frequent recurrences of fever, due to fresh attacks of bronchitis or bronchopneumonia, or to other than disease of the respiratory organs. Emaciation, loss of strength, night-sweats, loss of appetite, and disturbed digestion are usually present. The breathing is labored, necessitating the patient's being propped up in bed, or he may have to sleep sitting in a chair. The right ventricle fails, as shown by cyanosis, enlargement of the liver, distention of veins, clubbing of the fingers, and even well-marked pulmonary osteo-arthropathy.

Later, cardiac dropsy supervenes, the urine becomes scanty and albuminous, weakness becomes so great that the bronchial secretion cannot be expelled, and death takes place from failure of the vital powers.

Besides the ordinary muco-purulent bronchitis which is much the most common, there are three other clinical varieties deserving of special notice.

1. *Dry Catarrh* (Catarrhe sec of Laennec).—Dry catarrh is of rather rare occurrence. Laennec considered it very frequent, but he probably included the cases of winter cough already described. Apart from winter cough it is an uncommon affection. From time to time in the muco-purulent variety there may be cessation of secretion and then the symptoms are those of dry catarrh.

*Dyspnœa* is marked, and there is severe paroxysmal coughing with a little sputum, which is found to contain numerous small, pearl-like masses of tough mucus, with pus cells and blood corpuscles in its meshes. Charcot-Leyden crystals and Curschmann's spirals are also often present. The cough often causes acute tearing pain referred to a spot at the attachment of the abdominal muscles to the lower margin of the thorax. Fothergill attributes the pain to the violence of the cough causing the tearing of a muscle fiber from its attachment to the periosteum.

On *auscultation* there are many piping rales with hissing sounds; there may also be moist and creaking rales. Later the dyspnœa becomes con-

tinuous, owing chiefly to the emphysema, which nearly always develops; the course is marked by paroxysms like those of asthma, in which the wheezing and piping rales are marked all over the chest.

2. *The Serous Form of Catarrh.*—The serous form of catarrh, also first described by Laennec, is rare. It is distinguished by the expectoration of profuse, mucoserous, translucent, colorless sputum, which separates into an upper frothy layer, and a lower clear one like egg albumen or gum arabic mixed with water. The rarity of this affection is shown by the few cases reported in recent years, and the variety in the descriptions given of it by different writers. West describes an acute and a chronic form. "As a primary disease the *acute* is very rare; but in a mild form it is not very uncommon in many pulmonary affections." It may appear as a suffocative catarrh, and in children prove rapidly fatal.

The *chronic form* is commonly preceded by ordinary catarrh, and, once established, it is usually intermittent. During the twenty-four hours several pints may be expectorated, often in copious quantities at short intervals. It may persist for years without change in character, and the patient's general condition be little affected. Some cases are probably of the nature of a nervous hypersecretion. It may occur as a terminal phenomenon in acute tuberculosis, acute pneumonia, pleuritic effusion, cardiac disease, etc. Occasionally a profuse serous discharge occurs in cases of thoracic aneurism or mediastinal tumor. It may occur after aspiration of a pleural effusion and give rise to extreme dyspnœa, which may prove fatal from filling of the bronchi with the serous fluid. The patient is drowned in his own secretion. The smallest quantity aspirated, followed by serous bronchitis, is reported by Riesman as 1800 cc.

3. *Purulent Bronchitis* (Bronchoblennorrhœa).—Purulent bronchitis is the third form described; it is more or less marked in the final stage of all cases of chronic bronchitis, but there may be a marked purulent sputum from the first, a pint or more being expectorated in the twenty-four hours, as if a large cavity or an empyema had ruptured into a bronchus. The pus may become offensive but the odor soon abates; the odor is less marked than in putrid bronchitis. Purulent bronchitis may become converted into the putrid variety, however, especially if bronchiectasis develops. As a rule the patients lose flesh early, but the course of the malady is usually chronic. West has seen an acute form develop in the course of typhoid fever. A pint or more of sputum was expectorated in twenty-four hours; the cases were not fatal, the symptoms disappearing with convalescence.

**Diagnosis.**—Careful and repeated examinations of the sputum afford the most reliable means for a diagnosis of chronic bronchitis and they rarely fail to guide to a correct conclusion.

*Asthma* is differentiated by the paroxysmal dyspnœa, the slight degree of cough, the scanty expectoration, and the peculiar characteristics of the sputum. In severe chronic cases, after bronchitis and emphysema have become marked, the diagnosis has to be made by the history.

In many *tuberculous cases* the diagnosis from chronic bronchitis is difficult. The sputum may not contain bacilli, and emphysema may obscure the signs of local changes. Disease in any part of the lungs, especially the apex, without apparent cause, is presumptive evidence of tuberculous infection. In doubtful cases a tuberculin test will generally give positive evidence if tuberculosis exists.

*Aortic aneurism* or *mediastinal tumor*, by pressure on the main bronchi, may cause symptoms that lead to a diagnosis of bronchitis as the primary affection; so may also stenosis of the trachea or main bronchi resulting from syphilitic disease.

*Emphysema* is distinguished by the shape of the chest, the expiratory dyspnœa, the loud resonance, the weak respiratory murmur with prolonged expiratory sound, the limited movement of the diaphragm, as shown by the Litten sign, and the fluoroscope.

Bronchitis secondary to *cardiovascular disease*, can be differentiated by examination of the heart and arteries. The history, the condition of the heart and arteries, and examination of the urine will indicate those secondary to renal disease.

**Prognosis.**—In the young the outlook is often hopeful, even when they are emphysematous and subject to attacks of asthma. Many improve as they grow older, and in time the symptoms may completely disappear. After middle life there are few recoveries, but many are able to lead comfortable, useful lives and may attain advanced age, unless carried off by some intercurrent affection. In the severer cases various complications are certain to arise in time. Of the complications general *emphysema*, the most common, is rarely absent. It increases the dyspnœa as well as the liability to recrudescences of the bronchitis.

*Interstitial fibrosis* of the lungs is common, and may lead to the gradual development of bronchiectasis. *Bronchiectasis* is, however, always preceded by weakening of the bronchial wall by inflammation. Much weight should be attached to the state of the cardiovascular system, as in the late stages the chief danger is from failure of the right ventricle.

**Treatment.**—There is no disease in which it is more necessary that "the patient and not the disease" should receive first consideration than in chronic bronchitis. The therapeutic indications are much less definite than in the acute affection, and therefore a variety of methods may have to be tried in the effort to suit the treatment to the individual. It is of the first importance to avoid a cold, wet, and foggy climate; but it is in just such climates that the affection is most frequent, and, unfortunately, most sufferers are unable to seek a better one. Those who have the means should live in the most favorable climate. A mild sea air is usually most beneficial in the winter, such as Nassau, Bermuda, Jamaica, Cuba, Florida, and Southern California in America; in Europe, the Mediterranean Coast, Sicily, Madeira, the Canary Islands, and the Isle of Wight.

Some patients, especially those with tuberculous tendencies, do better in a dry, warm climate, such as Mexico, New Mexico, Arizona, and Colorado; and in the East the higher parts of Georgia and the Carolinas. Not rarely it will be found best to try moist and dry climates alternately.

In the summer months a more bracing climate will usually be found most beneficial if a continuous outdoor life is led, especially in the forest districts or on the plains. In Canada, Muskoka, the forests of Northern Ontario and Quebec, the plains of the Northwest, the foot-hills of the Rocky Mountains, and many parts of British Columbia offer admirable opportunities for such a life. In the United States, the New England and the Pacific Coast States are the best. Experience has proven that all these parts afford excellent resorts for tuberculous patients, and they should be equally favorable for chronic bronchitis, but as yet little consideration has

been given to the subject. In time it will probably be shown that in chronic bronchitis, as in tuberculosis, the all-important matter in the treatment is not the mild climate, but the outdoor life, care being taken to keep the body and limbs warm so as to prevent congestion of the bronchial mucous membrane. Even in the Yukon, long-standing cases of chronic bronchitis have quickly recovered.

If the patient is unable to leave home, no effort should be spared in improving the general condition. This will necessitate as much outdoor life as possible. The clothing should be light but warm so as to prevent chilling of any part. Mouth breathing should be avoided, and, if necessary, a respirator worn to warm the air.

The closest attention should be given to the functions of excretory organs, so as to counteract the strong tendency that exists in many of these cases to the accumulation of waste products in the blood. These products impede the circulation and increase the labor of the heart and act as irritants to the bronchial mucous membrane. The diet should be ample for the needs of the patient, but excess should be avoided. Cod-liver oil, if it does not disturb appetite or digestion, benefits many, especially those of spare habit.

The *cough* is usually more frequent in the morning, less so on lying down at night, and not rare during the night; it is often relieved by giving bicarbonate of soda in warm milk. At Brompton Hospital a combination of sodium bicarbonate, gr. 15 (1 gm.); sodium chloride, gr. 5 (0.3 gm.); spirit of chloroform, ♏ 5 (0.3 cc.), in anise-water, added to an equal quantity of warm water, is the usual combination administered. If the sputum is scanty and viscid, ammonium carbonate and potassium iodide, of each gr. 3 (0.2 gm.), may be added.

Hydrotherapeutic measures suitable to the individual case are regarded by the German physicians as the most effective of all methods of treatment. These measures are best carried out at a properly equipped institution, but many of them can be utilized at home. Full warm baths of long duration repeated from time to time are efficient aids in lessening secretion and making it more easily expelled. They will effectually replace much of the expectorant medication. In connection with the hydrotherapeutic measures, much benefit is found from courses of alkaline or sulphur waters.

If frequent acute attacks occur, they are to be treated as already indicated in acute bronchitis. The more depressing remedies are, however, rarely advisable and should not be given to the feeble or the old. If the secretion is viscid and scanty, the use of alkaline fluids in a fine atomizer, better the nebulizer, may give much relief. If not effective, inhalations of the vapor of hot water to which have been added one or more of the volatile remedies —creosote, eucalyptol, menthol, compound tincture of benzoin—may be tried.

These and similar drugs may also be given internally. Terebene, ♏ 10 (0.7 cc.), is probably the most valuable if expectoration is profuse. Turpentine, ♏ 10 (0.7 cc.); creosote, ♏ 2 to 3 (0.13 to 0.2 cc.), and terpene hydrate, gr. 2 to 5 (0.13 to 0.4 gm.), are also much used.

Copaiba is regarded by many as the most effective of the balsams. Its volatile principle is eliminated by the respiratory mucous membrane, modifies its secretion, and acts to a certain degree as an antiseptic. Tar has been recommended as an addition, gr. 4 (0.25 gm.) of each being given in capsule four to eight times a day. Balsam of Peru and of Tolu, benzoate of soda,

galbanum, ammoniacum, and many others have also been used, as in this formula:

| | | |
|---|---|---|
| Turpentine, | | |
| Purified tar . . . . . | āā | ʒss (2.0). |
| Balsam of Tolu . . . . . | | ʒiss (6.0). |
| Benzoate of soda . . . . . | | ʒiiss (10.0). |

For eighty pills: eight per day.

All these remedies produce similar results. If badly borne by the stomach they may be administered by inhalation. A spray or the dry fumes of chloride of ammonium is often of much use. Wine of ipecacuanha is highly spoken of by Ringer and Murrell. These remedies may be used as an addition to the turpentine group.

In long-standing and inveterate cases, intratracheal injections may be used as recommended in bronchiectasis. Menthol in olive oil, 5 to 10 per cent., is useful; if there is much odor, iodoform may be substituted for the menthol. Ichthyol should also prove useful. The *postural method* described under bronchiectasis should greatly aid in expelling the secretion when abundant and in preventing dilatation of the bronchial tubes. Such a *posture* during the night, as will prevent the accumulation of secretion in the bronchi, is one of the most valuable aids in the treatment. If the foot of the bed is well raised, so that the upper part of the chest is lower than the base, the drainage of the secretion from the bronchi will not only secure undisturbed rest, but will also relieve the mucous membrane of the continued irritation of its own secretions, one of the chief causes of the persistence of the inflammation. The position should soon cease to be irksome.

Many of the more volatile antiseptic remedies may be used in a dry inhaler. An oronasal respirator is efficient if the state of the breathing is sufficiently good to permit the patient to wear it. It may be worn each day, several hours at a time.

Local applications to the chest, using either cold compresses or linseed poultices, with or without mustard, according to indications, are advisable. In the intervals between the attacks, liniments are usually preferred, such as tincture of iodine, ʒss to j (2 to 4 cc.) to the ounce (30 cc.) of liniment of turpentine, applied at night until moderate irritation is produced.

The Turkish bath, or a portable hot-air or vapor bath in the bed-room if used promptly at the beginning of an intercurrent acute or subacute attack, often aborts it. It should be followed by a warm bath. A full warm bath of itself may be equally effective; it is more easily given and in the aged less likely to cause depression. The feeling of oppression and tightness in the chest is greatly relieved as soon as the perspiration appears. After the bath the patient should be rubbed dry and at once put into a warm bed in a warm, well-ventilated room. A respirator may be worn during the night, the sponge being lightly saturated with terebene, menthol, or eucalyptol. These and similar measures, especially hydrotherapeutic ones, will go far to obviate the necessity for internal medication.

Sulphur and arsenical thermal waters have been found useful in both the dry and purulent forms of chronic bronchitis and are much resorted to in Europe.

These measures usually suffice to control the cough if it is due to the secretion rather than to excessive irritability of the mucous membrane. In the latter case something having more sedative effect will be needed.

The addition of 15 to 20 drops (1 to 1.4 cc.) of chloroform to the inhalation may sufficiently moderate the cough; if not, one of the bromides may be added to the warm alkaline mixture already specified. If this is insufficient, heroine or codeine will have to be given until the cough is sufficiently controlled, due caution being taken, however, that necessary cough is not interfered with; or paregoric, a time-honored remedy, may serve the purpose better, as the camphor stimulates the circulation of the debilitated and the aged. Whisky at bedtime, especially in the aged, often serves the double purpose of quieting the cough and causing refreshing sleep.

General treatment is required as indicated, in each individual case. Iron, quinine, strychnine, cod-liver oil, glycerophosphates, etc., may aid in improving the general health, and, in so far as they do so, in lessening bronchial secretion.

The digestive organs should receive careful attention. Owing to the general weakness and the loss of muscular tone and fat, gastroptosis is apt to occur, followed by gastric atony with its train of symptoms resulting from protracted retention of the contents of the stomach. The diet should therefore be suited to the digestive powers of the individual as determined by a careful investigation.

The treatment of asthmatic attacks occurring in the course of chronic bronchitis will depend on their character. The more purely spasmodic they are, the more effectively will morphine hypodermically relieve them, but it is a dangerous remedy if there is much secretion. In the latter cases, "the drugs of greatest value are potassium iodide, gr. 8 to 15 (0.6 to 1 gm.); extract of stramonium, gr. $\frac{1}{4}$ (0.016 gm.), and the ethereal extract of lobelia, ♏ 20 (1.3 cc.), in combination with stimulant expectorants, such as carbonate of ammonia, gr. 3 to 5 (0.2 to 0.4 gm.), or ether" (Fowler).

As there is general venous fulness a saline purgative sufficient to cause a free action of the bowels will be of much benefit.

In those in whom there is damage to the heart, the greatest dependence must be placed on cardiac stimulants and tonics. Digitalis is the best of the stimulants, and it should be taken in short courses from time to time. Exercise in the open air, but not beyond the powers of the patient, so as not to overstrain the heart, is probably the best of all cardiac tonics. Respiratory gymnastics are of much benefit; as are also daily cold baths, provided they are followed by a feeling of exhilaration. Similar treatment is called for in the corpulent, in whom also the bronchitis is due to defective circulation.

In alcoholics, the failure of circulation is the chief cause of bronchitis, but toxæmia is also an important one. In their treatment, in addition to improving the vigor of the heart's action, it is necessary that alcoholic drinks be much reduced or cut off, and the digestion and excretion restored as far as possible to a healthy state. In all cases of defective excretion, natural salicylate of soda or salicylic acid is useful in rendering the bile more fluid and increasing the quantity excreted.

In the advanced stage of chronic bronchitis with dyspnœa and cyanosis from failure of the right ventricle, temporary relief may follow a rapid venesection, ten ounces or more of blood being taken quickly in a full stream in order to rapidly lower the distention of the ventricle. Cardiac and general stimulants, such as strychnine, digitalis, caffeine, ether, and alcohol, should be given according to the individual needs. Inhalations of oxygen may give much relief.

If respiration is impeded by the accumulation of secretion in the bronchi and suffocation is threatening, an emetic may afford temporary relief through the act of vomiting expelling the secretion. In the debilitated condition of these patients it is a dangerous remedy; it should not be resorted to in the more feeble, lest it produce fatal depression. As in all these cases there is labored expiration due to emphysema, compression of the chest during expiration by the hands applied over the axillary regions should be made several times a day to assist in expelling the secretion, as recommended by Ewart. This should be carried out while the patient lies prone with the shoulders hanging over the side of the bed or couch. The *posture* during the night already described, if assumed, should prevent this accumulation of secretion.

Of the value of compressed-air baths there is a diversity of opinion. They have been much used in Europe, but have now, Hoffmann says, "almost disappeared from ordinary practice." They are only a system of respiratory gymnastics, and for this purpose simpler methods may answer equally well.

*Respiratory gymnastics* of any form are valuable in chronic bronchitis. They should be carried out in air that is pure and free from dust, as in the forests and at the sea-shore. They are best carried out without apparatus, as they can be taken at any time and in any convenient place. Deep inspirations followed by long and forced expirations will prove useful exercises to anyone who patiently perseveres in their use.

**Secondary Bronchitis.**—Bronchitis is a frequent complication of a variety of diseased conditions. As a rule the symptoms and physical signs do not differ from those ordinarily met with in primary bronchial affections. It is not necessary therefore to do more than point out the relationships of these various diseases to the etiology of the bronchitis and their influence on its course and treatment:

1. **Bronchitis in the Course of Febrile Diseases.**—In *measles* some degree of bronchitis is always present, so that it may rightly be considered an essential part of the disease. As the smaller tubes are usually affected, it is from the bronchitis with its complications, especially bronchopneumonia, that the chief source of danger arises in many cases.

In *typhoid fever* slight bronchitis is of such frequent occurrence in the initial stage of the disease that it may be regarded as caused by the typhoid toxin. By some this initial bronchitis has been attributed to the early localization of the typhoid bacillus in the bronchial mucous membrane. Late in the disease, when the heart becomes weak and adynamia pronounced, bronchitis may be the occasion of much anxiety; it is caused partly by the toxæmia and partly by the defective circulation. The symptoms in such a case are due to hypostatic congestion as well as to the bronchitis. There is much danger of bronchopneumonia from extension of the inflammation.

As a sequel to *whooping-cough*, bronchitis with collapse of lobules is frequent; it may cause a paroxysmal cough similar to the original disease. The bronchitis of *influenza* is of special importance owing to its frequency of occurrence and its influence on the course and mortality of the influenza. The mucous membrane of the trachea and bronchi shows the usual changes of acute catarrh. The secretion, especially of the smaller tubes, at first is viscid and often blood-stained. The inflammation is very prone to extend to the deeper structures of the bronchial wall; this accounts for the frequency with which influenzal bronchitis is followed by bronchiectasis.

The occurrence of bronchitis varies in different epidemics of influenza, as well as in different persons in the same epidemic. It has been a more frequent symptom of late years. It may occur early, beginning as a coryza. Cough is usually frequent, short, dry, and very distressing. It is very persistent and difficult to relieve. The expectoration may be very scanty throughout, or it may become free as the attack advances. It is often adhesive and scanty at first, but may become muco-purulent and copious later.

The severity of the general symptoms will depend upon the extent and size of the bronchi affected. If the inflammation extends to the capillary tubes the respiratory symptoms will be severe and it will be difficult to determine that bronchopneumonia has not developed.

The *physical signs* are those of bronchitis with very adhesive exudate, and are therefore usually not marked. Sibilant rhonchi may be present. When the smaller tubes become affected, a high-pitched "piping" or "hissing" rale may be heard at the bases. The bronchitis may, however, affect only a small area and be localized in any part of the lung, not rarely in the apex; in such cases it is liable to be regarded as tuberculous. It may be difficult to differentiate the condition from acute miliary tuberculosis unless examination of the sputum shows tubercle bacilli.

*Treatment.*—The treatment does not differ from that of other forms of acute bronchitis. There should be due appreciation of the gravity of the affection, of its long duration in all marked cases, and its liability to terminate in chronic bronchitis and bronchiectasis.

2. **Bronchitis of Gout.**—This is of the chronic recurrent form affecting the larger tubes. The etiological relationship is so clear that many gouty persons recognize it themselves and often take advantage of the warning to forestall an arthritic attack. The bronchitis usually precedes, but may follow, an attack or occur during its course. The bronchitis often occurs as a morning cough usually quite out of proportion to the expectoration, which consists of a small quantity of yellow secretion. Piping rales may be present and the breathing is often "wheezing." As the gouty age is after middle life there is usually more or less emphysema present.

Fowler describes another form of gouty bronchitis met with in middle-aged persons and characterized by sudden onset and more severe symptoms, with marked cardiac disturbance. There may be marked dyspnœa and cough, and the presence of fine, bubbling, and crackling rales, chiefly at the bases of the lungs; fever may be slight or absent. These symptoms may be followed by an acute arthritic attack, or they may subside under treatment without further manifestations of gout.

In persons subject to gout chronic interstitial nephritis is liable to develop; and then similar attacks of bronchitis may occur from the pulmonary congestion and œdema caused by the cardiac changes associated with the renal disease.

3. **Bronchitis in Heart Disease.**—This is of great importance, both as a sign of the existence of the affection of the heart and of the impending failure of its function. Three varieties have been distinguished: the bronchitis of mitral affections, of aortic affections, and a form occurring in cases showing myocardial, arteriosclerotic, and valvular lesions.

Of these, the bronchitis in *mitral insufficiency* is the one most often seen and most important. It generally affects both lungs and is chiefly due to

hypostatic congestion. It is characterized by small, moist rales which are marked at the base, and diminish rapidly from below upward. There is ordinarily a small quantity of effusion into the lower part of the pleural cavities. It is a bronchitis of progressive character, slow in development, and without sudden accessions. It causes gradually increasing dyspnœa exaggerated by slight exercise, in marked contrast to the nocturnal dyspnœa of asthma with emphysema. The cough is variable but fatiguing even when not severe. The sputum is muco-purulent and varies in quantity; in it are found the so-called *cardiac insufficiency cells*. These are large cells containing reddish or rust-colored pigment from blood; in health these cells contain black pigment. They probably come from the alveoli, as they resemble the epithelium normally found there. They are found almost constantly and in such numbers in hypostatic congestion from heart disease that they have been regarded as quite characteristic. They are said to be sometimes found in small numbers in various conditions of the lungs, but not constantly or in abundance.

In *mitral stenosis* there are frequently recurring attacks of bronchitis in many cases. At first these attacks are slight and the expectoration consists of frothy mucus; later it often becomes tinged with blood. If the right ventricle becomes well hypertrophied so as to maintain a high degree of tension in the pulmonary vessels, free hæmoptysis is frequent and may prove fatal. In such a case known to be due to mitral stenosis, at autopsy the pulmonary arteries were found the seat of marked atheromatous degeneration, and greatly dilated even to their smallest branches. The right ventricle was very greatly hypertrophied but not dilated.

In the *diagnosis* of the bronchitis of mitral stenosis the error is often made of mistaking it for pulmonary tuberculosis, chiefly on account of the hemorrhagic sputum, but also because of the anæmia, absence of cyanosis, and late dropsy of mitral stenosis. A careful examination should suffice to prevent the mistake.

Bronchitis occurring in affections of the myocardium and of the aortic orifice and in the course of arteriosclerosis has been described. It is probably due, in the early stage, to renal disease, and later to cardiac failure, which is in reality relative mitral insufficiency. Huchard's *bronchite à répétition de la myocardite scléreuse* is apparently of the same nature.

Lasègue says "the bronchitis of mitral affections (insufficiency) is due to venous stasis, passive, indolent; the bronchitis of aortic affections is due to active arterial hyperæmia and occurs in paroxysms." If "*renal affections* before cardiac failure" were substituted for *aortic affections* the contrast would probably be correct and would be as striking.

*Treatment.*—The treatment should have for its first object the improvement of the circulation, as the chief danger is from failure of the heart. The patient should therefore be placed at rest, and the diet should be dry in order to add as little as possible to the volume of the blood, which is already too great. Heart tonics and stimulants, especially digitalis, will be required to strengthen the heart and increase excretion by the kidneys; purgatives will be of use chiefly by lessening the volume of the blood. In conditions of weak and irregular heart with sleeplessness, morphine hypodermically is usually the only effective heart tonic, and its use is seldom attended with danger in this form of bronchitis. Potassium iodide may do much good by acting on the bronchial mucous membrane, rendering the expectoration

easy and quieting the cough, and at the same time acting favorably on the myocardium. If there is œdema, diuretin or theocine may be effective in strengthening the heart and stimulating the kidneys. The diet should be salt-free.

4. **Bronchitis in Renal Disease.**—Three forms of bronchitis in renal disease have been described by Lasègue: 1. A simple and common form attended by migratory and fugitive bronchopulmonary œdema. The cough is slight, but dyspnœa of greater or less degree requires treatment. This dyspnœa is paroxysmal, but is not increased by movement, and is worse at night than in the day, often attaining a severity sufficient to cause orthopnœa —the so-called renal asthma. On careful auscultation over one or several areas, crepitant rales are audible; these areas are not confined to any part, but may be found in the upper lobe, at the base, or in the axillary region. They never occupy a whole lobe. The rales are fleeting and may change from place to place during prolonged auscultation; rarely they persist in the same place for several days. If localized at the apex they simulate tuberculosis. This form occurs without fever, and is of short duration, but may recur with great facility. It may occur at the commencement of albuminuria or at any time during the course of the disease in a latent case.

2. The second form constitutes what is properly called *albuminuric bronchitis*. It occurs in chronic cases, develops suddenly, and may attain great intensity. The dyspnœa is intermittent and paroxysms are frequent. The cough is frequent, increased during the paroxysms, and accompanied by muco-purulent expectoration, often with blood intimately diffused or in filaments. This form occurs without fever, disappears after a certain time, and is liable to recur.

3. The third form gives the impression of a veritable *bronchopneumonia*. The onset is often brusque, with fever. The cough is severe and frequent, and increases for several days. The expectoration is abundant and sometimes sanguinolent. The oppression is marked and continuous, with paroxysms. On auscultation there are generalized bronchitic rales; after these disappear areas of persistent crepitation are still left. The affection begins in the large and descends to the small tubes, thus showing that the persistent areas are pneumonic. In the final stage of chronic nephritis, when the patient is nearly moribund, a diffuse congestion and œdema often occur, with large, moist rales, due to the stasis of the mucus in the bronchi, and caused chiefly, if not wholly, by cardiac failure.

**The Causation of the Bronchitis of Cardiac and Albuminuric Affections.**—The causes in these two affections are closely allied. The passive congestion and œdema occupy the bases of the lungs; they are the mechanical result of the enfeeblement of the heart that is the rule in cardiac cases, and is frequent in chronic nephritis.

The variable and fleeting congestions and œdemas are evidently due to *vasomotor disturbances*. In chronic nephritis they are doubtless caused by toxins acting on the vasomotor nerves of the bronchi and lungs, or on their centres in the medulla. In the cardiac cases they are apparently of analogous origin, the poison exciting them being partly due to renal insufficiency, and partly the carbonic acid in the blood due to mitral insufficiency.

*Renal asthma* is a term of very uncertain significance and applied to dyspnœa arising from a variety of causes. Occasionally in chronic nephritis there are paroxysms of dyspnœa that cannot be distinguished from true

asthma and are probably due to the same cause. But the term renal asthma is not confined to these cases, but applied to all kinds of dyspnœa occurring in chronic nephritis in which sudden attacks of difficult breathing, especially at night, are quite common. These attacks are often caused by the uræmic poisoning, but probably more frequently by the disturbed circulation in the lungs and nervous system arising from heart failure. Bronchitis in some degree always co-exists and aggravates the dyspnœa in both the uræmic and cardiac cases.

The treatment is such as is best for the renal affection: milk diet if there is no œdema, otherwise dry diet; free action of the bowels; potassium iodide in suitable cases. These means usually ameliorate the bronchitis as well as act favorably on the renal affection. Dry cupping of the chest may do much good, many cups being applied to all parts of the chest, front and back. They may be repeated two or three times a day. Sedatives are often injurious. As cardiac affections usually co-exist with the renal, both conditions should be considered in the treatment.

## TUBERCULOSIS OF THE TRACHEA AND BRONCHI.

Tuberculous infection of the trachea and bronchi is generally regarded as secondary to pulmonary tuberculosis and is not usually treated of as a separate disease. In the trachea and at least the larger bronchi the disease is a rare one except near the end of life, and even then it is far from frequent. This relative immunity is accounted for by the following conditions: (1) The trachea and bronchi form simple, smooth, open tubes, whose walls never come into contact nor present any irregular cavities in which the sputum can lodge and be compressed. (2) Their surfaces are protected by a layer of mucus which is being constantly moved upward by the strong ciliary motion of the epithelium, carrying along with it all foreign substances that have lodged on it. For this reason the surface never presents any deposits of carbon particles, even although the respired air be laden with them. (3) The ciliated epithelium is highly irritable. Catarrhal inflammation and a heavy coating of mucus lessen their activity and hence reduce their protective power (Kraft). (4) The tracheal and bronchial mucous membrane is highly sensitive and excites reflex cough when irritated by foreign substances.

For these reasons primary tuberculosis of the tracheal and bronchial mucous membrane is very rare; and in the pulmonary affection it usually escapes because the sputum is hurried along so rapidly as to prevent infection of the healthy membrane, and render it infrequent even in the abraded areas, which are usually protected by a thick layer of mucus. Toward the end of life irritability is lessened and the sputum, travelling more slowly, destroys more frequently the less resistant epithelium, so that the bacilli often find an entrance. The posterior walls are injected most frequently because in the bedridden they are the more exposed.

The tuberculosis of children is essentially a tuberculosis of the small bronchi. This is indicated by the frequency of the disease in the bronchial glands and by the rarity of hæmoptysis, of chronic, circumscribed, apical consolidation, and of cavity formation. The strong tendency to tuberculous bronchopneumonia is further evidence of the bronchial invasion.

Two processes have been demonstrated pathologically, viz., tuberculosis of the bronchi and tuberculous or caseous bronchitis. Clinically, neither one of them is known, both being obscured by the more important pulmonary symptoms which always co-exist. Rindfleisch regards the terminals of the bronchioles as the point of most frequent infection, but probably somewhat larger branches are also not rarely infected. The bronchial wall becomes infiltrated with small cells, causing considerable thickening, and the area of infiltration is soon converted into a yellowish-white, well-defined mass. The epithelium becomes destroyed early, and the mass, unless the process becomes arrested and absorption takes place, degenerates and is discharged into the bronchus, leaving a small, caseous ulcer. The tendency of the process then is to penetrate more deeply and excite peribronchial inflammation and later involve the lung tissue itself.

*Leprosy* also occurs in the bronchi, and presents changes similar to those of tuberculous bronchitis.

## SYPHILIS OF THE TRACHEA AND BRONCHI.

Nothing definite is known of the occurrence of the secondary lesions of syphilis in the trachea and bronchi, either as mucous plaques or condylomatous masses. The laryngoscope has revealed red, slightly elevated patches like the macular and papular eruptions on the skin, which have rapidly disappeared under treatment. A few instances of syphilitic tumors have also been observed to disappear under treatment. These lesions doubtless occur likewise in the bronchi and give rise to some degree of irritation with symptoms of bronchitis.

Tertiary lesions are associated frequently with disease in the larynx, also with affections of the lungs, liver, etc. The lesions are most frequent near the bifurcation, occurring both in the trachea and bronchi. The gumma varies in size from that of a pinhead to a walnut. One or several may be present, or the deposit may be diffuse in the mucous membrane. It infiltrates all the coats of the bronchus, even the cartilages becoming affected. The swelling rarely causes sufficient stenosis to disturb respiration, the symptoms being those of subacute or chronic tracheitis and bronchitis, with more or less profuse purulent expectoration, which is occasionally blood-stained, especially in the ulcerative stage. The ulceration extends as deeply as the infiltration, so that healing may be followed by extensive scarring that may cause much deformity. The gummatous infiltration may be circumscribed and lead to ulcers and scars, or diffuse and cause widespread destruction of the mucous membrane and diffuse perichondritis. The first condition is found chiefly in the larger bronchi and often causes hæmoptysis; the second follows the course of the bronchi and invades the lungs, causing considerable cirrhotic change. The two forms, however, are not sharply separated but merge into each other.

**Symptoms.**—The symptoms are those of ordinary bronchitis. In some cases there is an unusual quantity of blood in the sputum. Gradually the symptoms of stenosis develop with increasing expectoration, which affords some relief when copious and bloody, but the symptoms grow worse when the sputum becomes scanty and only muco-purulent. In some cases instead of the symptoms of stenosis those of hectic fever occur, and the condition

then simulates pulmonary tuberculosis, hence the name "phthisis syphilitica." If secondary tuberculous infection takes place it may completely overshadow the original disease. Various complications, especially bronchiectasis and bronchopneumonia, are quite frequent.

**Diagnosis.**—The diagnosis is not difficult if there is a clear history and the throat shows the usual signs of the disease. In the absence of these guides, the diagnosis is not easy, tuberculosis being especially difficult to differentiate. Tubercle bacilli if present in the sputum do not necessarily exclude syphilis, as tuberculosis may occur as a secondary infection. All the diseases causing stenosis will have to be considered before arriving at a diagnosis of a syphilitic lesion.

**Treatment.**—The treatment should be vigorous, mercury and potassium iodide being given freely. They should be given even in developed stenosis, the object being to remove all recent exudate about the scar. The stenosis may be explored by the bronchoscope and, when possible, appropriate surgical treatment adopted.

## FIBRINOUS OR PLASTIC BRONCHITIS (PSEUDO-MEMBRANOUS BRONCHITIS).

This affection is characterized by the occurrence of a coagulable bronchial exudate from which are formed cylindrical or solid casts of the bronchial ramifications. It is a rare affection. Up to 1869 Lebert was able to find only 44 undoubted cases in the literature. In 1889 West found 54 more cases, and Bettmann in the literature from 1869 to 1902 found 145 cases (including West's), making, with Lebert's list, 189 in all. Since then up to September, 1905, there have been 12 undoubted cases recorded in the *Index Medicus* up to May, 1907.

To these the writer can add 3 unreported cases: 1 from the Museum of the Medical Department of the University of Toronto, 1 of extensive casts associated with hæmoptysis occurring in the practice of W. J. Wilson, of Toronto, and 1 at present under the care of T. McKenzie.

The occurrence of casts was known to Hippocrates, Galen, and other ancient authors, although incorrectly interpreted.

**Etiology.**—This affection may occur at any age, but is probably rarest in old people. Like bronchitis, it is most common in cold, damp climates, and therefore in the cold seasons of the year.

In diphtheria it may occur as a sequel to disease of the fauces and larynx, especially the latter. The reported cases, however, are not numerous probably because the complication has often been regarded as a matter of course, and therefore not calling for a special report. In 220 autopsies, Councilman, Mallory, and Pearce found definite membranous deposit in the bronchi in 42 subjects. Although usually secondary, a primary fibrinous bronchitis may doubtless also be caused by the Klebs-Loeffler bacillus.

Fibrinous bronchitis occurs in association with a great variety of diseases, so various, in fact, that the association appears accidental. The largest number have been met with in persons affected with pulmonary tuberculosis and heart disease, but these two affections are of such frequent occurrence that too much importance should not be attached to this association. It has been met with in the course of the various infectious diseases, such as

pneumonia, measles, scarlatina, erysipelas, typhoid fever, variola, articular rheumatism, and influenza. A few cases have occurred in association with asthma and some with pulmonary œdema following thoracentesis. Inhalation of irritant fumes and gases, as smoke, steam, and ammonia, has been the cause in some cases. A few cases have been reported as occurring in connection with severe pemphigus affecting the skin and the mucous membranes of the mouth and throat; the affection has been regarded as essentially a pemphigus of the bronchi.

An apparent relation of fibrinous bronchitis to menstruation has been observed. In a case of Graves' disease a fibrinous exudate occurred during the administration of potassium iodide. Then there are some cases for which no cause can be assigned, primary idiopathic cases. These may occur in robust, previously healthy people.

With the exception of diphtheria and pneumonia, we are not certain that the affections with which the occurrence of the fibrinous exudate is associated bear a causative and not an accidental relationship; the association would seem to be merely a coincidence.

**Special Pathology.**—Little is known as to the pathology of fibrinous bronchitis. It seems certain that a variety of agencies may cause a membranous exudate. There is no doubt that the pneumococcus and diphtheria bacillus may cause membranous exudate in the bronchi as elsewhere, but whether other microörganisms cause it also is uncertain. It is also uncertain whether all cases are due to bacteria, as no microörganisms can be found in some specimens. The exudate may form solid casts of the bronchi, or hollow cylinders, or both may be present in the same case. The casts from the small bronchi are probably always solid and from the larger ones hollow. The inclusion of air bubbles may give the casts a beaded appearance. The exudate may be produced in a few bronchi only, or occur in several areas in one or both lungs. Nearly all the casts in museums have been coughed up, few being found in the bronchi at autopsy.

Casts vary in length from an inch or so up to six or seven inches, with branches corresponding to the divisions of the bronchi from which they are expelled. They are pearly gray or white in color, the larger firm and the smaller softer in consistence. The larger are laminated, the inner layers showing foldings due to the forcing of the older layers farther and farther from the bronchial wall and toward the centre of the tube, by the successive deposits on the mucous membrane beneath them. The terminal casts are spiral in form, and the sputum may contain Curschmann's spirals, Charcot-Leyden crystals, and eosinophilic cells, indicating a condition of the mucous membrane similar to that in asthma. The casts usually consist chiefly of fibrin; some are of mucus, but many are found of both in varying proportions. In the meshes of the laminæ are found epithelium, Charcot-Leyden crystals, fat globules, and, in the outer layers, sometimes blood corpuscles.

Marfan describes three classes of casts: (1) In pneumonia and acute, idiopathic, fibrinous bronchitis the casts are yellowish. They are solid, but show imprisoned air bubbles. They consist of leukocytes and fibrin, and are designated leukocyto-fibrinous casts. (2) In diphtheritic bronchitis the casts are white, opaque, and often hollow. They are composed chiefly of fibrin and degenerated epithelial cells—*fibrino-epithelial casts.* (3) In chronic pseudo-membranous bronchitis the casts are white, transparent, and often hollow; they are *muco-albuminous, fibrinous,* or *fatty.*

The condition of the bronchi is uncertain. The epithelium must be destroyed to some extent, but the destruction may be limited to small areas.

**Symptoms.**—Dyspnœa, cough, and the expectoration of casts are the essential symptoms, the presence of casts in the sputum being the characteristic one. The onset is variable. The affection may set in suddenly, but usually there are symptoms of a catarrhal bronchitis for a longer or shorter time before the attack develops.

In the cases with more acute symptoms there is usually an expectoration of mucous secretion before the casts are expelled.

The dyspnœa is caused by the obstruction produced by the casts and will vary in proportion to their size, number, and rapidity of formation. Its onset may therefore be gradual or sudden. With the expectoration of the casts the dyspnœa is generally relieved, to recur again as the casts are reformed. In the acute cases the dyspnœa is often continuous with exacerbations, while in chronic ones it occurs during the attacks only, the breathing in the intervals being quite free. A number of cases are reported in which there was little or even no dyspnœa, the membranes being expelled without difficulty and the patient's general condition being little disturbed.

The sputum, apart from the casts, is catarrhal in character, and may amount to a pint or more daily. On the other hand, it may be scanty. The casts usually appear as masses or pellets, their form only becoming apparent when they are floated in water. Their number may be few or many daily, depending upon the extent of the bronchial implication, the rapidity with which casts reform, the looseness of their attachment, and hence the ease with which they can be expelled, and the force of the cough. They are not rarely expectorated more freely at night. Blood is quite frequently present in the sputum, and amounts to a hæmoptysis in about one-third of the cases. The hemorrhage occurs quite apart from tuberculosis, and is the result, not the cause, of the fibrinous bronchitis. It is apparently due to the rupture of vessels in the bronchial wall caused by the tearing away of the membrane through the violence of the cough. Some observers, however, doubt the possibility of the bronchial vessels being the source of such profuse hemorrhage. It may precede, accompany, or follow the expectoration of the casts.

The cough may be mild, the membrane being brought up with ease, or it may be of any degree of severity. When most laborious and severe it may bring up little secretion. At times a peculiar flapping sound caused by the partial separation of membrane is heard during coughing.

Fever may be present in acute cases, but there is nothing characteristic in its course. It may be remittent, with sweating, and there may be loss of flesh, so that pulmonary tuberculosis may be simulated and can only be differentiated by the subsequent history. Even in protracted cases the general health may continue good. Albuminuria is present in some cases in which there is severe dyspnœa, and is doubtless due to venous stasis in the kidney.

The physical signs are generally very indefinite, there often being no more present than those of chronic bronchitis. The respiratory sounds may be weakened or even absent over areas in one or both lungs, owing to obstruction by the membrane. There may be rhonchi or sibili, and moist rales of all sizes may be heard, and occasionally flapping sounds produced by partially separated membrane. If occlusion of bronchi occurs from the fibrinous deposit, or obstruction by separated membrane, there may be

signs of pulmonary collapse, as absence of breath sounds, dulness on percussion, and diminished expansion of the chest. If cough leads to the expulsion of the casts these signs may suddenly disappear as the lung is again expanded.

The following case in the practice of T. McKenzie, from whom the history was obtained, is an excellent example:

The patient was a female, aged twenty-seven years. The bronchial attack for which she first sought advice in November, 1905, began in the late summer. She had a dry, irritating cough, with little sputum, and at times coughed severely for several days, when she vomited some white substance. During the consultation she had a severe paroxysm of coughing and brought up a cast, receiving it into her handkerchief without being aware of its existence until it was shown to her. The bronchitis continued until February and during this time she had four marked paroxysms, in one of which she coughed up almost a complete cast of the bronchi of the lower lobe of the left lung, one considerably larger than the one shown in the illustration, Fig. 29. In the intervals between the paroxysms the sputum consisted of a moderate quantity of milky fluid containing small white masses of membrane. All the paroxysms in the morning began with chilly and shivering sensations, and in the afternoons there were hot flushes and chilly feelings. Her throat was dry, the cough was irritating, and increased by the slightest exertion. After a day or two casts would be brought up and she would improve and promise a speedy recovery. But a slight cough continued and the physical signs over the lower part of the left lung persisted. There was slight but varying dulness, most marked before and diminishing after the expulsion of the casts. Coarse crepitation was audible, beginning about the middle and continuing to the end of inspiration, apparently due to the separation of the casts; it resembled a coarse, exaggerated crepitation of pneumonia. The temperature varied from subnormal to 100°; the pulse was rapid, especially during the paroxysms; sleep was disturbed by the cough and soreness across the middle of the chest. There has been no recurrence since February, 1906, and her health has improved materially.

FIG. 29

Cast from a case of fibrinous bronchitis.

**Diagnosis.**—In typical cases there is no difficulty in diagnosis; the casts by themselves leave no room for doubt. From *asthma* there may be much difficulty in diagnosis, and in all doubtful cases the sputum should be carefully searched for pellets and masses of rolled-up casts. A small *foreign body* in a bronchus causes similar attacks, but the history and relapses of

fibrinous bronchitis will prevent error. *Diphtheria* is to be excluded by the bacteriology and the absence of membrane in the fauces and of laryngeal symptoms. In *pneumonia*, as in diphtheria, casts may also occur, but the history and physical signs usually leave no room for doubt. In *bronchitis* the occurrence of an attack of dyspnœa and the absence of respiratory sounds over an area of lung, with but slight impairment of the percussion note, might be considered sufficient for a diagnosis, but to make it certain the sputum should be carefully searched for casts.

**Prognosis.**—A fatal result is rare in an uncomplicated case. In Fagge's case the loosened cast became lodged at the tracheal bifurcation and caused death by asphyxia. In the rare form in which acute attacks follow one another in rapid succession, death may occur during a paroxysm, usually within one or two weeks from the onset of the disease. Extensive deposits in the bronchi doubtless occur in such cases.

The marked tendency to recurrence is to be borne in mind. The intervals between attacks may be short or long, and liability to them may continue for many years.

**Treatment.**—The value of any treatment in a disease that runs such an uncertain course as fibrinous bronchitis is difficult to estimate, as any relief following recourse to it may be the natural course of the disease, uninfluenced by the treatment. Potassium iodide is the only drug regarded as of material value by English and American writers. It should be given in full doses. Mercurials seem to have little influence on the affection, even when given freely. Water vapor, especially that from lime-water, is highly valued by German observers. If it reaches the membrane it will certainly have a solvent effect on it. It should be most effectively applied by means of a nebulizer. Creosote in vapor, or in the nebulizer, continuously inhaled may prove of much value. Intratracheal injections of oil, plain or medicated, have been used. Ewart reports a favorable result in a case in which creosoted oil (1 in 20) was dropped at intervals through a tracheotomy tube. Injections may be given by Mendel's method or without difficulty by injection through the glottis.

The general management of these cases should be guided by the principles on which the treatment of simple bronchitis is carried out. In dyspnœa, the inhalation of oxygen may give relief and aid in sustaining life until the cast is expelled, but in most cases, fresh cold air will probably be found more agreeable as well as more efficacious. The associated conditions, of which cardiac disease and pulmonary tuberculosis are the most frequent, require suitable treatment. Claisse obtained notable improvement by the use of Marmorek's antistreptococcic serum.

## FŒTID OR PUTRID BRONCHITIS (GANGRENOUS BRONCHITIS).

Fœtid or putrid bronchitis is a rare affection. It is not a definite disease, but only a peculiar form of decomposition which may occur in the secretion in any disease of the lungs or bronchi; it may be a passing phenomenon in any form of chronic bronchitis.

**Etiology.**—Fœtid bronchitis is always a secondary affection which only develops in bronchi previously altered by *acute* or *chronic bronchitis, bronchiectasis, chronic tuberculosis*, or by *foreign bodies* in the bronchi. It is

probable, therefore, that the microörganisms which cause the putrefaction are able to develop only on mucous membrane whose epithelium has already been injured or destroyed. Those most liable to the affection are such as those whose vitality is depressed by privations, alcoholism, and malnutrition from any cause. The definite microörganisms that give rise to the decomposition have not been determined; many are found in the secretion and probably several may be able under varying conditions to cause it. Bacteriology has not, as yet, added much to our knowledge of the condition.

The *Oïdium albicans* has apparently been the cause in some cases, the decomposition following exposure to thrush infection. Cases are reported in which *Leptothrix pulmonalis* and *Bacterium termo* have been found in abundance in the secretion. From the sputum of a case of fœtid bronchitis, four varieties of staphylococcus, a diplococcus, and a bacillus were isolated, and possibly each of them was able to cause decomposition. *Bacillus coli communis* is said by some to be the usual microbe of gangrenous bronchitis, and a germ called the *Bacillus putidus splendens* has been described as pathogenic (Bernabei).

**Special Pathology.**—The morbid changes are few and not constant. The medium-sized and small bronchi are chiefly affected. The diseased bronchial wall is reddish, wine-colored, or pale gray. The epithelium is cast off, and on scraping the surface with a scalpel a soft, fœtid pulp is exposed. In many places the wall of the bronchus is destroyed and the process extends to the peribronchial tissue; it may lead to the formation of actual gangrenous cavities. Thus putrid bronchitis is not only an almost constant complication, but also a frequent cause of bronchial dilatation.

The process may terminate (1) in complete recovery or in bronchiectasis; (2) in fatal chronic septicæmia or in abscess of the brain; (3) in extensive gangrene of the lung.

**Symptoms.**—The characteristic symptom is the horrible, gangrenous odor of the patient's breath and sputum; it often permeates the room and even the whole house. The sputum is remarkable for its abundance, especially if there is bronchiectasis, amounting in many cases to several ounces in twenty-four hours. It is muco-purulent in character, and ordinarily separates into three layers. The *upper layer* forms the greater part of the sputum; it is frothy and greenish. It consists of mucus, holding in its meshes many pus and epithelial cells. The upper part contains many air bubbles, and from the lower surface many brownish flakes hang down into the fluid below. The *second* layer consists of dirty, greenish, thin fluid, incorrectly called serum. The *third* layer is formed of sediment of various kinds: detritus, fat drops, and peculiar, horribly offensive pellets known as Dittrich's plugs. These plugs vary in size from a microscopic point up to a bean; they contain fat needles, leptothrix, leucin, tyrosin, and fine granules from degenerated cells. These plugs were first described by Dittrich; Traube regarded them as characteristic.

*Cough* is frequent, but not severe, as the sputum is brought up in large quantity with ease. *Fever* is present in many cases, and, being septic, is a serious symptom. It is probably due to the absorption of putrefactive products.

The disease usually begins rather suddenly and is essentially paroxysmal. In strong persons it may disappear after one or many weeks, leaving the patient uninjured. It recurs not infrequently. In severer cases septic symptoms rapidly develop, often beginning with chills. Signs of prostration

soon follow, and the patient passes rapidly into a typhoid state. Cough and expectoration cease and death in collapse follows.

In some cases complications occur, such as ulceration and gangrene of the lung, and bronchopneumonia, with diffuse bronchitis. In others, metastatic fœtid abscesses form in various organs. The disease presents a very varied history, and the descriptions of the earlier writers varied according to the kind of cases seen. Thus Trousseau describes a relatively mild class, while Traube, Sée, and Andral give the details of cases of great severity which were usually rapidly fatal. Sée proposed the name of septic bronchitis for such cases.

**Diagnosis.**—The difficulty of diagnosis consists in excluding other affections giving rise to fœtid expectoration. It is usually an easy matter to exclude the condition in which the fœtor is due to disease above the larynx, that is, in the nose, mouth, or pharynx. When the cause lies below the larynx, however, it may be impossible to be certain that the fœtid discharge does not come from bronchiectasis, a gangrenous cavity in the lung, or a gangrenous abscess in the mediastinum or elsewhere in the thorax. In fact, a putrid bronchitis apart from one of these conditions is very rare, so rare that its existence has been questioned, although a few cases, with autopsy, have been reported. It is scarcely possible, however, in any case of putrid bronchitis to exclude bronchiectasis with certainty.

In *gangrene* of the lung, the onset is more sudden, hæmoptysis is usually of frequent recurrence, and shreds of pulmonary tissue will probably be found in the sputum; elastic fibers are not often found, as they are rapidly dissolved in the gangrenous fluid.

Fœtid expectoration may result from the rupture into a bronchus of an empyema, of an abscess of the vertebræ, the lung itself, or the liver; or of a subdiaphragmatic abscess due to appendicitis or other abdominal disease. In all these conditions symptoms usually develop suddenly without preceding bronchitis, and the source of the pus may be evident on examination. On the other hand, a diagnosis is often impossible; even a postmortem examination may leave it in doubt.

**Treatment.**—To maintain the best possible general condition and correct the fœtor usually sums up the utmost that can be done. For the former, pure outdoor air is of the first importance; then rest or exercise such as each case requires, sufficient nourishment, and the necessary tonic and stimulating remedies accomplish all that we are able to do for the general health. For the fœtor, inhalations of antiseptic vapors are usually the most effective remedies. The best deodorant is probably creosote given by inhalation. Inhalations of turpentine have long been resorted to and are often useful. Both remedies may be given internally. West regards musk, a grain in a pill, or an equivalent of the tincture, given three times a day, as the most efficacious remedy. Intratracheal injections of antiseptic remedies should also be effective.

## BRONCHIECTASIS.

The first description of this affection was given by Laennec, whose attention was directed to it in 1808 by his assistant Cayol, then a student. Laennec, however, does not seem at first to have appreciated the importance of the condition, and it was not until 1825 that his first description of it was published.

**Etiology.**—The variety of pulmonary conditions with which bronchiectasis is associated makes it difficult to assign the cause and manner of its production. There has been therefore the greatest variation in the explanations offered. All are agreed, however, that the affection cannot develop in a healthy bronchus, but only after some pathological process in its walls has weakened their powers to resist pressure. Inflammation of the bronchi, to be effective in causing dilatation, must be destructive; it must destroy the structure which gives resisting power to the bronchial wall, viz., muscular tissue, elastic tissue, and cartilages. Such damaging effects do not occur in ordinary catarrhal bronchitis, because the deeper structures of the bronchi are not affected, but they are liable to be produced by the infectious lesions of the bronchi which occur in bronchopneumonia, acute or subacute. Dilatation of the bronchi is especially liable to develop in the bronchitis and bronchopneumonia of influenza, and also, although probably to a less degree, of whooping-cough and measles. Dilatation almost uniformly results after the entrance and lodgement of a *foreign body* in a bronchus.

Leichtenstern reports many cases of acute bronchiectasis of the middle and smaller bronchi in influenza, as proven on *postmortem* examination. In many instances, cases presenting the same signs as the fatal ones, terminated in recovery even after many months. The bronchitis in some was diffuse, affecting most of the bronchial ramifications; in others it was limited to parts of one lung and quite sharply defined. Such localization is an important peculiarity of the bronchitis of influenza and may render it difficult to distinguish it from tuberculous infection. After an attack of influenza has run its course, if numerous large metallic rales with copious sputum of a bronchiectatic character persist, the percussion note at the same time remaining normal, the existence of bronchiectasis is probable. Such cases with bronchial dilatation may last for months and yet recovery be complete.

Lord[1] published a most interesting report of 11 patients with chronic influenza, of whom 2 died, 1 recovered, and 8 continued to cough, with persistence of influenza bacilli in their sputum. In one of the fatal cases the autopsy demonstrated diffuse bronchiectasis. The sputum had constantly shown the presence of influenza bacilli. In the other fatal case the influenza bacilli were present in the sputum for a month and then disappeared. Death occurred two years later, but no autopsy was done. Of the 8 cases, all had abundant sputum containing great numbers of influenza bacilli mixed with other organisms, but with the constant predominance of the influenza microörganism; there were no tubercle bacilli. In all probability these were all cases of bronchiectasis and due to deep infection of the bronchial walls by influenza bacilli.

Another report of great interest is published by Boggs[2] from the Johns Hopkins Hospital. There were 6 cases, of which 2 were fatal. In 5 of them the influenza bacilli were obtained in pure culture from the sputum; in 1 there were a few influenza bacilli present, but pneumococci predominated. In the 2 fatal cases, at the autopsy, marked dilatation of the bronchi extending to the periphery was found, and the bacilli were obtained in pure culture from the secretion and from the deep tissues of the bronchial wall.

[1] *Boston Medical and Surgical Journal*, vol. ciii, No. 19, pp. 537–540, and No. 20, pp. 574–579.

[2] *American Journal of the Medical Sciences*, November, 1905, vol. cxxx, p. 902.

PLATE II

Bronchiectasis. (Carswell.)

In the bronchitis of whooping-cough the deeper structures of the bronchial walls are not rarely affected, and, not being able to resist the high pressure caused by the cough, dilatation occurs.

When bronchopneumonia is so intense as to destroy the muscular and elastic fibers on which the strength of the bronchial wall depends, there is also at the same time such inflammation of the surrounding lung tissue that it becomes sclerosed in time, so that the two lesions are associated—dilatation of the bronchi and sclerosis of the peribronchial pulmonary tissue. In general conditions which lower the vital resistance of the organism, there is greater probability that bronchopneumonia will cause dilatation of the bronchi and sclerosis of the peribronchial lung tissue. Such conditions are met with in alcoholics, the poor with insufficient food and unsanitary surroundings, and in rachitic subjects. These conditions greatly lower the vitality of the tissues, lessen their reaction to irritation and their power of repair, and so favor the termination of acute in chronic processes.

FIG. 30

Section of lung showing dilatation of the bronchioles. (Transactions of the Pathological Society of London, vol. liii.)

Dilatation of the bronchi may, however, occur as an acute process and be general throughout both lungs. Fletcher[1] reports such a case in a child, aged three years, who died nineteen days after the onset of bronchitis. A week after the onset the breathing was very short and cough painful and excessive. On admission the child was fat, but had slight signs of rickets. The temperature was normal and the respirations from 80 to 90 per minute. The cough was short and severe; the movements of the chest free and equal; there was no inspiratory recession; crepitant and rhonchial rales were audible all over both lungs. The percussion note was normal. At the *autopsy* the lungs were voluminous, their surfaces densely studded with transparent bullæ in size from a pinhead to a small pea, but no consolidation or collapse was present. The cut surface was densely riddled with hemispherical spaces, giving it a honeycomb appearance (Figs. 30 and 31). There were no

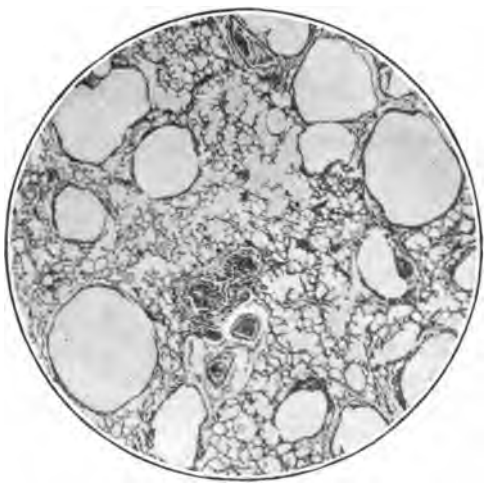
[1] *Transactions of the Pathological Society of London*, vol. lii, p. 193

tubercles. Microscopic sections showed acute bronchitis with desquamation of epithelium and small-celled infiltration of both large and small bronchi. The spaces were formed by bronchiectatic cavities.

No *age* is exempt from the occurrence of bronchiectasis. However, it is rare in nurslings, as they usually succumb to bronchopneumonia in the acute stage, or even to such bronchitis as would cause dilatation of the bronchi. The affection is frequent in children after the age of three years and in adolescents. It occurs also in adults and in the aged. It is more frequent in men than in women.

*Tuberculosis*, formerly regarded as antagonistic to the development of bronchiectasis, is a frequent cause. In *chronic fibroid phthisis* in which there is much peribronchial sclerosis, typical bronchial dilatation of greater or less degree is practically constantly present. In *ulcerative phthisis*, dilatation of the bronchi is associated with the cavity formation. In these cases the terminal bronchi are affected and the dilatations are small.

FIG. 31



Microscopic section of Fig. 30. (Transactions of the Pathological Society of London, vol. liii.)

In *stricture of the bronchi*, dilatation occurs above and below the seat of contraction; that above is regarded as due to the force of inspiration, and that below to the force of expiration. In these cases there is not only destructive inflammation of the various coats of the bronchial wall, but also implication of the peribronchial pulmonary tissue, which in time becomes sclerosed. *Syphilitic disease* may be the cause of the bronchial stricture.

**Pathogenesis.**—There is much difference of opinion as to the mode of production of bronchial dilatation, but all are agreed that the affection is a secondary one. It is generally preceded by chronic disease of the dilated bronchus, and associated with this there is, as a rule, sclerosis of the lung and pleura.

The various opinions as to the mechanism of dilatation may be grouped into two classes:

1. Those which regard the causes acting within the bronchi as playing the principal or essential role.

2. Those which regard lesions external to the bronchi (*a*) of the lungs and (*b*) of the pleura, as taking a part in causing the dilatation.

Some observers regard all three classes of causes as acting unitedly to produce the bronchial dilatation.

1. **Causes Acting within the Bronchi.**—The view which is generally adopted to account for the dilatation of the bronchi rests upon two principal factors: (*a*) lesions in the bronchial wall by which its power of resistance to pressure

is diminished, and (*b*) increase in the intrabronchial pressure by expiratory effort, with partial or complete closure of the glottis, especially in coughing, but also in crying and singing.

The expiratory pressure of cough may easily rise to 80 mm. of mercury, and in severe coughing 110 or more may be reached; in quiet expiration it does not exceed 2 or 3 mm. This shows the very great variations of pressure to which the respiratory tract may be subjected. Violent cough must always cause distention of the bronchi and may appreciably increase their caliber, from which the elastic and muscular tissues in health cause an immediate recoil. Such sudden increase of pressure is the common cause of emphysema; weakened parts of the bronchial tree must yield under similar circumstances if their power of resistance is less than that of the pulmonary tissue. The increase of pressure alone, even when sudden, as in cough, does not of itself suffice to cause bronchial dilatation; lesion of the bronchial wall diminishing its resistance is also essential. The chief strength of the bronchial walls, in which the cartilages do not form complete rings, depends upon the tonicity of its muscular and elastic coats. Inflammatory processes in the bronchial tubes may extend deeply in places and partly or wholly destroy the elastic and muscular fibers and so weaken the resistance of the bronchial wall, that it yields to the ordinary pressure of air without the influence of cough or strain. The injury and loss of the muscular and elastic fibers have been shown to occur at the seat of dilatation and there only. Stokes in 1841 pointed out that inflammation of a serous or mucous membrane paralyzed the subjacent muscular layers. It is therefore probable that the majority of cases of ordinary bronchiectasis are due to the expiratory pressure of cough acting on areas of bronchial walls whose elastic and muscular coats have been partly or wholly destroyed by infection from chronic bronchitis.

*Stenosis of Bronchi.*—Narrowing of bronchi is a very frequent cause of dilatation; it is always associated with chronic bronchitis, at least in the neighborhood of the narrowed part of the bronchial tube and the inflammation always invades the deeper structures. The narrowing may be due to the pressure of an aneurism or a new-growth, to cicatricial contraction of a gumma in the bronchial wall, or to the entrance and lodgement of a foreign body. However produced, the obstruction or narrowing is followed by dilatation beyond the site of constriction and often on the proximal side as well, the former caused by the pressure of expiration and the latter has been attributed to that of inspiration, probably incorrectly. The extent of bronchus affected by dilatation will coincide with the extent of bronchial walls weakened by the inflammatory process, and the degree of dilatation will depend on the degree of injury to the walls and of pressure to which it is subjected.

2. **Causes External to the Bronchi.**—(*a*) *Pulmonary.*—Corrigan[1] first described *cirrhosis of the lung* and considered it the usual cause of bronchial dilatation by the contraction of the new fibrous tissue dragging on the bronchial walls. But Charcot pointed out that dilatation of the bronchi occurs only as a sequel to bronchopneumonia in which there is destruction of the muscular and elastic coats of the bronchi, and never in simple sclerotic changes in the lung.

[1] *Dublin Journal of Medical Science*, 1838.

*Collapse of the lung* from any cause is frequently followed by bronchiectasis, especially in children, in whom, however, the collapse generally results from capillary bronchitis, which no doubt injures the muscular and elastic structures of the bronchial wall. Collapse of lung resulting from obstruction of a bronchus also aids in the production of bronchial dilatation. All these pulmonary affections, however, play only an accessory part.

(*b*) *Changes in the Pleura.*—Thickening of the pleura is the rule in bronchiectasis, but this does not prove that it is effective in the production of the dilatation. Moreover, the two conditions occur quite independently of each other. Wilson Fox has suggested that the two affections, when they co-exist, probably develop simultaneously, and that the bronchial dilatation is not due to the thickened pleura and the fibrosis of the lung which accompanies it, but to the high intrabronchial pressure arising from the cough acting on the weakened bronchial walls.

Briefly, then, lesions of the bronchial wall are necessary to the development of bronchiectasis, but the frequent co-existence of pulmonary and pleural lesions suggests that they are important accessory causes.

Hoffmann regards stenosis as the one factor that is preëminently frequent as a cause of bronchiectasis. He cites Traube's and Lichtheim's experiments showing that occlusion of a bronchus, if followed by purulent inflammation, leads to dilatation; but if it remains aseptic there is no dilatation, although the corresponding part of the lung becomes atelectatic. Partial occlusion by admitting air, and with it pyogenic organisms which cannot be easily expelled on account of the obstruction, will therefore favor the development of bronchiectasis even more than complete occlusion, notwithstanding that atelectasis is not so likely to occur.

In partial occlusion of a bronchus, the air during inspiration passes through the stricture and distends the bronchus, filling the space beyond it. In expiration, the secretion lying in the tube may be disturbed so as to completely close the narrowed part and prevent the escape of the air. If the expiration is obstructed as in coughing, the plug may be forced back by the increased intrabronchial tension and more air driven into the weakened tube, further distending it. Then the secretion may again act as a ball-valve and obstruct the egress of the pent-up air. The weakened bronchus is thus subjected to constant high pressure which is from time to time suddenly increased by the excessive pressure developed in the expiratory act of coughing.

**Morbid Anatomy.**—On opening the chest of a subject who has died of bronchial dilatation the lungs are found distended, the pleuræ are thickened and adherent, and the lung tissue itself indurated. In places there is marked emphysema. In mild cases in which the dilatations are small and usually few in number, the lung appears normal. In many of these cases it is not until the bronchi are laid open longitudinally that the dilatations can be demonstrated. In very marked cases, the diseased lung, on section, presents a characteristic appearance, resembling a sponge, or if more consolidated, the wall of the gravid uterus with dilated venous sinuses.

**Varieties of Dilatations.**—Bronchiectasis is usually described under two varieties, the *cylindrical* and the *saccular*. They are often associated in advanced cases. The cylindrical form sometimes tapers toward its extremities, resulting in a fusiform dilatation. Occasionally a series of dilatations occurs in a tube, producing a bead-like appearance—the *moniliform*.

Other classifications have been made, but none of them enable us to gain a clearer conception of the condition.

*The cylindrical dilatations* occur chiefly in the larger tubes and those of medium size; they may extend to the surface of the lung. The tube is rarely regularly dilated, but usually presents irregular constrictions and dilatations depending on the varying strength of the different sections of the bronchial wall. At the constrictions there is generally increase of fibrous tissue which has contracted, often in some places forming an incomplete septum. The dilatations represent the thinner and weaker portions of the bronchus. The dilatation often terminates suddenly, less often gradually, in a normal bronchus. The distal end may become further dilated into a bulbous enlargement, especially when surrounded by emphysematous lung. If the cylindrical dilatation tapers toward the extremities, it becomes *fusiform*. Although the cylindrical dilatations affect the bronchi of the third and fourth order, they may extend and end abruptly beneath the surface of the lung. Their existence may be evident on the cut surface of the lung by the increased number of orifices from which large quantities of mucopus well up. In many cases, however, they are not evident until the bronchi are laid open; this is especially the case if only a few tubes are affected. These limited degrees of bronchiectasis are most frequently found below the root of the lung and downward toward its base. They are also met with in association with local areas of emphysema.

The *saccular* form presents an appearance in striking contrast to the cylindrical. In this variety the terminal bronchi are often affected, the alveoli opening into them dilate, their thin septa atrophy, and small cavities are produced similar to those of emphysema. The section of the lung shows the appearance of a cavernous tissue formed by smooth, shining-walled cavities, with a small, circular opening at the bottom of each, the bronchial tube of which the saccule is a bronchiectatic dilatation. A whole lobe or even a whole lung may be affected, and resemble in appearance the lung of a turtle—"turtle-lung," Gruyére—"cheese-lung." "In all likelihood, if the parenchyma of the inflated lung could be cleared away so as to expose the tubes in their continuity, each would be found changed into a regular series of globular dilatations, so as fairly to deserve the epithet *moniliform*" (Fagge). In some of the smaller cavities the openings at the bottom are not apparent or easily found; sometimes on account of their being filled with inspissated secretion; such cavities have been described as closed cysts. However, in many cases the sac is in reality without any exit, as its bronchus has become obliterated and converted into a fibrous cord.

The size and number of the cavities vary very much. They may be as large as a small orange, in which case they are few in number and the structure of the bronchial wall can be demonstrated with difficulty. As a rule they do not exceed one-half an inch in diameter; then they are more numerous and situated nearer the surface of the lung. In the early stage their size is microscopic. Not rarely all forms of bronchiectatic cavities, cylindrical, fusiform, and saccular, are found in the same lung.

In cases of advanced bronchiectasis the pulmonary tissue has generally become markedly fibrosed. In portions of lung showing an earlier stage of the affection, and doubtless in more recent cases, the saccules are smaller and not crowded so closely together, but separated by normal lung tissue containing healthy bronchi.

**The Extent of the Affection.**—At the commencement it is usually confined to a few bronchi of one lung, the left more frequently than the right. In course of time it is spread more widely by cough, inspiration of secretion into unaffected tubes, recurrent attacks of bronchitis to which all cases are liable, and the not infrequent attacks of inhalation pneumonia.

At the *postmortem* examination, many bronchi are usually found affected, varying much, however, with the duration of the disease. In 54 cases, Lebert found one lung only affected in 28, and both lungs in 26 cases. In 35 cases of Fowler's, both lungs were affected in 23, and the disease was confined to one lobe in 8 only. The situation is determined chiefly by the cause. It is most common in the lower lobes because the greater number of determining causes—bronchitis, bronchopneumonia, and chronic pleurisy—affect the bases of the lungs. For the same reason in cases resulting from tuberculous disease, the apex is most commonly affected.

**Structure of the Walls of the Bronchi in the Neighborhood of the Dilatations.**—To the naked eye the appearance of the dilated bronchi presents a different aspect, according as the lesion is recent or of old standing. If the lesion is recent the cavity is lined by mucous membrane showing the changes due to chronic bronchitis; it is glistening and of reddish color and the glands appear to be atrophied. Below this are to be seen plaques of cartilage, and occasionally elastic and muscular fibers, giving the tissue a striated appearance. If the dilatation is old the mucous membrane is more or less granular or even covered with papillomatous vegetations; sometimes it is traversed by pearly bands of connective tissue, producing a trabecular appearance. In some cases the membrane is soft and presents a pultaceous, gangrenous aspect, emitting a stale or fœtid odor similar to that of the muco-purulent secretion lying in the dilated cavity.

On the cut surface of the lung the transverse sections of the thickened bronchi in the cylindrical variety stand out prominently, in striking contrast to the thin-walled tubes usually found in saccular cases. The tubes may be filled with muco-purulent secretion of extremely fœtid odor and of varying consistence. The secretion consists of mucus containing many pus cells and desquamated epithelial cells from the bronchi and alveoli. Blood is sometimes present, and a variety of bacteria and fungi. If partially shut off from the external air the secretion may become inspissated and form a mortar-like mass from the deposit of calcium salts and fat crystals; the formation of broncholiths is but a further step in the process. They may be confounded with the cretaceous products of tuberculosis. If the bronchus is occluded so that air cannot enter, the dilated tube may be filled with clear, odorless, yellowish fluid, in which a faint growth of bacteria may appear, resembling the contents of a culture tube.

In the apex of the lung a tuberculous cavity that has discharged its contents may closely resemble a simple "bronchial dilatation." "Close inspection will show (1) that the bronchus opens into the cavity too abruptly for bronchiectasis, (2) that the bronchial mucous membrane can only be followed over a small surface immediately adjoining the orifice of the bronchus, and (3) that the wall of the cavity presents none of that sculptural detail which identifies the original structure of a bronchus even in extreme dilatation" (Ewart).

The microscopic appearances of the wall vary according as the dilatation is recent or of old standing; also as the section is taken from the middle or

either end of the dilatation. If the lesion is recent the epithelium is preserved; it rarely retains its cilia. Generally the epithelium is cubical or caliciform, or it may consist of long, fusiform cells. If the secretion is markedly purulent the mucous membrane may be covered by one or two layers of small round cells.

The submucous connective tissue is thick and infiltrated with round cells, and the infiltration extends into the perilobular connective tissue, which is always sclerosed in the neighborhood of the bronchial dilatations. The glands, the elastic and muscular fibers, and the cartilages enclosed in the connective tissue are always altered. The glands and their excretory ducts may be distended with round cells.

The muscular fibers have also wholly or in great part disappeared and it is to the loss of tone resulting from the disappearance of muscular fibers that the dilatation of the bronchus is attributed. The results found vary according to the part of the wall of the dilatation that is examined. From the equator or middle part of the dilatation, where the lesion is most advanced, the *muscular fibers* are found to have *wholly disappeared*, but toward either end of the dilatation they are preserved to a greater or less degree. In the dilatations of long standing the *epithelium* has wholly disappeared, leaving the surface of the cavity covered by coarse granulation tissue. In this tissue the capillaries become greatly dilated, sometimes uniformly, at others irregularly so as to form fusiform or sacculated aneurisms. It is to these changes that the hæmoptysis occurring so often in bronchiectasia is due.

In the majority of cases the bronchi that have not become dilated are the seat of chronic catarrhal inflammation.

**State of the Lung.**—In bronchiectasis the lung is always the seat of chronic inflammation that varies in degree according to the duration and extent of the bronchial affection. *Pneumonia*, lobar or lobular, may precede the bronchial dilatation, both the lung and bronchi probably being infected at the same time. A pneumonia which does not completely resolve may terminate in fibrosis of the affected portion of lung, and with this affection bronchial dilatation is frequently associated. It may be impossible to differentiate such a condition from local tuberculous disease. In bronchiectasis of long standing pulmonary tissue is sclerosed so that the lung is shrivelled, indurated, and impermeable to the air. On section it may creak under the scalpel. In the majority of these cases it is probable that the affection begins as a bronchopneumonia, the infection of the various coats of the bronchi destroying their muscular and elastic fibers and rendering them so weak that they yield to the pressure caused by coughing, and the infection of the lung terminating in chronic inflammation, followed by fibrosis, which is most marked in the peribronchial tissue. By some observers the dilatation of the bronchi is attributed, at least in part, to the traction by fibrous bands passing from one bronchus to another or to the thickened pleura. While fibrosis of the lung from any cause is frequently associated with bronchial dilatation there are still many such cases in which no bronchiectasis occurs. In the cases associated with bronchiectasis, it is much more probable that with the onset of the pneumonic process there is also deep infection of the bronchial wall, causing destruction of the muscular and elastic fibers, and that, as usual, the weak bronchi yield to the strain of coughing. The traction of the new fibrous tissue may cause irregularities in the dilatations and leads at places to occlusion of bronchi.

**Changes in the Pleura.**—Bronchiectasis is quite often associated with pleurisy with effusion, especially empyema. The effusion causes collapse of a part or the whole of the lung, and there may occur fibrosis of the interlobular and interalveolar connective tissue and dilatation of the bronchi. Wilson Fox has suggested that all these changes proceed simultaneously, and that even in these cases the dilatation of the bronchi is due to the distending force of the cough acting on the weakened bronchial wall, and not to the fibrosis of the lung.

**Differentiation of Bronchiectases from Tuberculous and Other Pulmonary Cavities Postmortem.**—It may be difficult at autopsy to distinguish bronchiectatic from tuberculous cavities. Tuberculous disease forms irregular cavities covered by caseous detritus and sometimes traversed by fibrous bands representing the vessels. Bronchial cavities are, on the contrary, of regular form, lined by smooth or granular membrane which represents the bronchial mucous membrane, ulcerated or not. Often one sees on the surface a striation due to the remains of muscular or elastic fibers, and can perceive bronchial cartilages deep in the wall.

The bronchi opening into the pulmonary cavities are ulcerated; on the contrary in the bronchial cavities their lining is continuous with that of the cavity. Around the tuberculous cavities there are tubercles in various stages of development; around the bronchial dilatation the tissue is carnified and sclerosed. The tuberculous cavities are generally situated at the apex of the lung, while bronchial dilatations occupy indifferent parts. However, error is often difficult to avoid, especially if the dilatations are small and develop at the bronchial extremities. In doubtful cases a search should be made for tuberculous deposits.

**Secondary Lesions of Various Organs.**—Perforation of the pleura and pneumothorax are doubtless often prevented by firm adhesions to the chest wall. Perforation into the mediastinum is a rare event; it would be followed by subcutaneous emphysema.

If the changes in the lungs are sufficient to obstruct the pulmonary circulation, failure of the right ventricle will result sooner or later and be followed by venous congestion, enlargement and congestion of the liver, and all the changes associated with these conditions.

The tracheo-bronchial glands are always enlarged, and may suppurate. Hypertrophic pulmonary osteo-arthropathy has been noted in a few cases. The kidneys may undergo chronic changes owing to the venous congestion, or become lardaceous, as in chronic suppurative diseases.

As a great variety of microörganisms, both pyogenic and saprophytic, are found in the fluid of the bronchiectatic cavities, secondary metastatic infections occur in many cases. Such secondary infections as suppurative hepatitis, abscess of the kidneys, septic inflammation of joint cavities, and osteomyelitis have been met with; but the most important and probably the most frequent localization is *abscess of the brain.* It often presents a gangrenous appearance and may exhale the same fœtid odor as that of the bronchial secretion. The meninges may become infected apart from cerebral abscess.

**Symptoms.**—Paroxysmal cough and copious, purulent expectoration, often offensive, are the chief symptoms of bronchiectasis. They occur most commonly on rising in the morning and on lying down at night; that is, change of position, if the cavities are full, causes dislodgement of secretion,

and this excites the cough and expectoration. The dilated, diseased bronchi have lost their normal sensibility to such a degree that contact of secretion does not excite cough, and it is not until the accumulated secretion is brought into contact with the more healthy mucous membrane by movement or change of position that cough results, usually with the expectoration of large quantities of purulent secretion, as much as 25 to 30 ounces (700 to 900 cc.) being expelled in twenty-four hours. Tolerance of this profuse and usually offensive secretion is remarkable; it rarely causes nausea or vomiting.

Expectoration may be free unless rendered difficult by advanced emphysema, fibrosis of the lung tissue in the neighborhood of the dilatation, or by stenosis of the larger bronchi. There is little cough in the intervals unless excited by associated conditions, especially emphysema. The site of the dilatation influences the cough. If the dilatation is in the upper lobe the drainage will be free, and there being little retention, the cough will therefore usually be relatively milder than when the lower lobes are affected.

The *sputum* is chiefly purulent; it is usually yellowish and has little adhesiveness. In general it is only after the case has been of some years' standing that the sputum begins to become offensive, and it may be some years more before the odor attains the horrible, fœtid character which is so marked in most chronic cases. The odor may be more marked in the breath than in the sputum.

After standing some hours the sputum usually settles into two or, more often, three layers: the lowest one of thick, purulent material containing various kinds of granular debris, and forming an opaque, gray mass; over this a thin, turbid fluid; and if there is a third one, an upper, thin, frothy, brownish layer. In the lower, dense layer there are to be found pus cells, granular detritus, many microörganisms, and on careful examination Traube's or Dittrich's plugs, which consist of fœtid, soft, grayish-yellow bodies formed in the smaller bronchi from the pus, detritus, crystals, etc.

Blood in the sputum is a late, but not infrequent, symptom. It is generally small in quantity and mixed with the secretion; but the bleeding may be profuse and repeated; it may even be fatal. It may be due to the ulceration in the wall of the bronchus eroding a branch of the pulmonary artery; this may occur without there being any tuberculous infection. An aneurism of a branch of the pulmonary artery sometimes forms and protrudes into a dilated bronchus; if it ruptures, profuse, even fatal, hemorrhage may result. Fowler met with this in two out of the three cases of death from hæmoptysis in bronchiectasis.

*Dyspnœa* is absent or slight in the early stages, but it usually increases as the disease advances and may become marked. It is then generally due to such complications as acute bronchitis, pneumonia, emphysema, cardiac dilatation, venous obstruction, ascites, etc.

*Pain* is not caused by the bronchial disease: when it occurs it is usually due to pleurisy occasioned by the nearness of the bronchial dilatation to the surface of the lung.

*Fever* may be absent throughout the whole course of the affection. In most cases, however, the course is marked from time to time by exacerbations of two or three weeks' duration, during which there is irregular elevation of temperature, increase of cough and expectoration, sweats, loss of appetite, etc. These attacks are probably due to fresh infections of the bronchi, the occur-

rence of new areas of bronchopneumonia, and to absorption of septic material from the decomposing bronchial secretion. In cases in which there is marked venous stasis from cardiac weakness the temperature is, as a rule, subnormal.

*Clubbing of the fingers* is of frequent occurrence, and is important as a sign of bronchiectasis. The toes may become similarly affected. In more advanced cases similar changes may occur also in the other phalanges, in the metacarpal bones, in the bones of the wrist and forearm, leg, etc., until finally all the peculiar changes of pulmonary osteo-arthropathy be presented.

As lardaceous or amyloid changes are prone to occur late in the disease, diarrhœa and albuminuria are then often met with.

**Physical Signs.**—Bronchiectasis may be secondary to such a great number of diseases, and such a variety of morbid changes may develop in its course, that there may be the greatest variation in the physical signs. The signs are those of the associated conditions rather than of the bronchial dilatation.

**Inspection.**—The chest may be enlarged and emphysematous, or, from fibrosis of the lung, it may be markedly retracted, and the heart more or less displaced.

**Palpation.**—Vocal fremitus and vocal resonance are increased over areas of fibrosis.

**Percussion.**—The percussion note will vary according to the degree of dilatation, its proximity to the surface, the condition of the surrounding pulmonary tissue, and the thickness of the overlying pleura. If a large dilatation lie near the surface, the percussion note will be dull while the cavity is full of secretion, but will become tympanitic as the secretion is expelled and the cavity fills with air. With the mouth open the tympanitic sound is more marked. Change of sound may occur with change of position, and metallic and cracked-pot sounds may be produced. Normal resonance immediately surrounding the seat of a cavity differentiates a dilatation from a tuberculous cavity, as the note is always dull in the vicinity of the latter. When many dilatations occur in close proximity, the note is usually raised in pitch and deficient in resonance, but the area is not usually definitely defined.

A cavity stationary in size points to bronchiectasis, while, as Stokes pointed out, an increasing excavation is preceded by consolidation and is peculiar to tuberculosis.

**Auscultation.**—In bronchiectasis with emphysema the respiratory sounds are vesicular with a tubular quality, but not cavernous. The sounds may be wavy, both in inspiration and expiration. When there is fibrosis around the dilatation, which is usual in the saccular variety, the vesicular breathing is lost and the sounds are definitely cavernous, usually with more or less "gurgling." Bronchophony and pectoriloquy may be marked. Skoda's "veiled puff" is often heard. This is a peculiar sound occurring at the end of inspiration; it gives the impression of a puff of air entering a small cavity situated just beneath the ear (Fowler).

The adventitious sounds are present in great variety. In the absence of fibrosis there are soft rales, both large and small, with sibili and rhonchi; if the lung is indurated they are higher pitched and crackling, or, more usually, coarse and metallic. They appear and disappear as the secretion in the tubes increases or lessens. Associated bronchial and pulmonary diseases produce a variety of rales which may obscure the signs of dilatation.

The movements of the heart not rarely produce rales. Loud, systolic

murmurs may be heard about the apex, in the back, and in the trachea and mouth.

**Complications.**—The cause of death is often a complication. Severe hæmoptysis, acute pneumonia, and bronchopneumonia are the most frequent. Gangrene of the lung in the neighborhood of the dilatation may occur and lead to a fatal termination. The diagnosis of such a complication is very difficult, as the odor and appearance of the sputum are similar in both affections. If, on microscopic examination, masses of pulmonary tissue are found, the existence of gangrene would be established.

A bronchiectatic cavity near the surface of the lung may rupture into the pleural cavity which was not obliterated by adhesion; empyema or pyopneumothorax will follow, and either is usually fatal.

Pyæmia is of frequent occurrence. In mild cases it may cause general malaise, with aching pains; in more severe infection various local infections may occur, such as abscess of the liver or kidneys, suppuration of joints, ulcerative endocarditis, and septic infection of the serous cavities. The most frequent of these metastatic infections is abscess of the brain.

In many cases death results from cardiac failure due partly to general weakness, but chiefly to obstruction to the pulmonary circulation caused by the fibrosis of the lungs.

**Diagnosis.**—A disease with so many associated morbid conditions, any of which may mask its symptoms, is always difficult of diagnosis. In no disease is the truth of this better illustrated than in bronchiectasis.

The repeated occurrence of sudden, profuse, muco-purulent expectoration, usually fœtid, with the rapid development of the signs of a cavity in an area previously flat, and followed by the gradual disappearance of these evidences of a cavity as the secretion re-accumulates, are strongly indicative of bronchial dilatation, especially if repeated over a long period of time. Some cases present this symptom-complex at frequent intervals, while in others, although closely observed for long periods, it is not found. Some patients are able to excite the discharge of secretion by assuming certain positions. A localized empyema rupturing into a bronchus may produce the same train of symptoms; this occurred in a patient under the writer's observation a few years ago.

The diagnosis from *tuberculosis* is usually readily made by the examination of the sputum except in the infrequent cases in which tuberculous infection occurs after the development of bronchiectasis. The history of the two diseases usually aids in reaching a correct conclusion. But the unusual cases are the ones that offer the greatest difficulty. As an example, the tuberculous process may begin in the lower lobe, or be secondary to a cured lesion of the apex that has escaped detection and thus closely simulates a bronchiectasis.

From *chronic bronchitis* with emphysema and profuse expectoration, especially if fœtid, the diagnosis is difficult, often impossible. The signs that indicate dilatation are: the periodic copious, fœtid, thin, muco-purulent expectoration; metallic or bubbling rales; areas showing altered percussion note, and the "veiled puff."

*Pulmonary gangrene* in patients with a history of chronic bronchitis may prove impossible of differentiation from bronchiectasis with ulceration and gangrenous destruction. Gangrene is usually sudden in onset and attended with more marked prostration, and it may be preceded by acute pneumonia,

bronchopneumonia, or tuberculosis. The occurrence of masses of pulmonary tissue in the sputum would prove the existence of gangrene.

In *circumscribed empyema* discharging into a bronchus, a diagnosis can, as a rule, be made without difficulty from the history and physical signs, but if the empyema forms between the lung and the diaphragm, or in the interlobar fissure, it may be quite impossible to distinguish it from a bronchiectatic cavity. A diagnosis is of importance, as in empyema an operation for drainage is necessary, a proceeding not admissible in bronchiectasis, except in the rare cases of single bronchiectatic cavity in the base of the lung; in these, operation has been successful.

If the cavity can be reached, the injection into it of a bismuth mixture may make it possible to determine by an *x*-ray examination the size, shape, and position of the cavity and of the bronchus through which its contents are being discharged.

A *new-growth* pressing on a bronchus, in some cases perforating it, or one growing from the bronchial wall, may give rise only to symptoms of bronchiectasis, the existence of which is due to the obstruction caused by the growths. Under such conditions the existence of the growth, even if suspected, could not be demonstrated.

As already pointed out, it is worthy of note that dilatation of the bronchi frequently follows chronic bronchitis caused by the influenza bacillus.

A protracted history of profuse fœtid expectoration which contains no tubercle bacilli or elastic fibers, of diffuse bronchial rather than circumscribed cavernous breathing, of coarse bubbling or metallic rather than gurgling rales, and, finally, of marked clubbing of the fingers, toes, and nose, points strongly to bronchiectasis affecting many tubes (Fowler).

**Prognosis.**—In the acute cases following measles, whooping-cough, and possibly influenza, in which the dilatation of tubes is only moderate, complete recovery will probably take place. In these, the peribronchitis, if it occurs, is usually only slight, and the inflammation abates before the muscular and fibrous tissues have been destroyed or seriously injured; nevertheless, many of these cases become chronic and may for years present the symptoms of bronchitis, affected by changes in the weather. A characteristic course is met with in well-marked cases in which there are no complications to influence the progress of the disease.

As to the duration of life, so much depends on the surroundings of the patient and the care which he receives that statistics are of little value. Cases lasting forty or fifty years are on record; again, many die within a year. The more diffuse the morbid processes causing the dilatation of the tubes, the greater the danger; therefore, the cases commencing in unresolved pneumonia or following collapse of the lung resulting from pleural effusion usually run a shorter course than those due to chronic bronchitis. The more frequent causes of death are bronchopneumonia, gangrene, hæmoptysis, and metastatic abscesses, especially cerebral. Other causes are tuberculous infection, venous stasis, dropsy from heart failure, and amyloid degeneration.

**Treatment.**—As our efforts to cure the dilatations are as yet ineffectual, we are reduced to the necessity of endeavoring to lessen the secretion and to keeping it as nearly aseptic as possible. The best means of accomplishing these objects is to have the patient live in absolutely pure air; this aids also in improving the general health. He must avoid crowded rooms because the air in them becomes impure. The greatest care must be taken to pre-

vent inflammatory processes of any kind, even the slightest catarrh of the respiratory tract.

In the attempt to render the secretion aseptic, use has long been made of inhalations of creosote, turpentine, carbolic acid, menthol, etc. These remedies have also been given internally. These methods of treatment are laborious, and have not been attended by gratifying success, chiefly because an insufficient quantity of the remedies reaches the affected tubes. However, during late years, success in several cases has resulted from the continuous inhalation of coal-tar creosote and the intralaryngeal injections of solutions of menthol, guaiacol, iodoform, creosote, etc., in olive oil, aided by the "postural" method. These remedies in sterilized oil have also been used as subcutaneous injections.

In the absence of any contra-indication, the patient should make systematic efforts at stated intervals to empty the cavities by assuming such positions, with the head lowered, as are found to promote the free discharge of the secretion. By emptying the cavity by such "postural" assistance he is relieved, to a certain extent, of toxic effects of absorption, and the cavity is the better prepared for the vapor or fluid that may be applied to it.

The protracted inhalation of creosote vapor was first suggested by Chaplin.[1] The object is to excite sufficient coughing to force out all secretion from the bronchi, and to secure efficient disinfection by the prolonged inhalation of the strong vapor of creosote.

In order to properly use the vapor, a small air-tight room should be set apart for the purpose, all openings about the doors and windows being packed with cotton-wool. In the centre of the room, on a pedestal, a spirit lamp is placed, and over it a flat, open dish is fixed and into it a sufficient quantity of creosote is poured. On lighting the lamp the fumes begin to rise and soon fill the room. At first only gentle heat is applied, the patient sitting in the room and inhaling the fumes. Later, the fumes can be inhaled with greater ease, and stronger heat may be applied so as to fill the room with dense fumes in which objects can scarcely be distinguished. As the patient can bear it, he may sit stooping over the dish and inhale the vapor as it rises. As the vapor is strongly irritant to the eyes and nose, they require to be protected. This can be done by covering the eyes with two watch-glasses framed in adhesive plaster, and plugging the nostrils with absorbent cotton. With such protection the patient can stand an inhalation with comparative ease that could not otherwise be endured. At first, from a few minutes to half an hour is sufficiently long for an inhalation; later, it may be borne for one or two hours.

To prevent the hair and clothing being saturated by the creosote vapor, a cap or towel should be put on the head so as to completely cover the hair, and an overgarment put on to protect the clothing. The floor, if wooden, should be protected by placing the pedestal on a stone slab or in a large tinned vessel, since the burning creosote may flow over the edge of the dish. A gas jet to heat the creosote is not safe as the supply tubing may be set on fire.

The effect of the inhalation is to excite violent paroxysms of coughing and cause the expulsion of large quantities of secretion, even although much has been expelled just before the inhalation began. This residual secretion

[1] *British Medical Journal*, 1895, I, p. 1371.

is usually horribly offensive from having lain long in the cavities. As the treatment proceeds, the expectoration usually changes markedly. At first profuse and fœtid, it becomes gradually lessened in quantity and the odor diminishes; in four or five weeks the quantity may be trifling and the odor slight. The respiratory capacity improves so that much greater exertion can be undertaken without dyspnœa. The patient's general condition grows better in every way; the temperature, if elevated, gradually becomes normal, and the pulse becomes stronger. The chest, on examination, shows evidences of empty cavities with few rales.

The method of treatment has the merit of being inexpensive and easy of application. Unfortunately, it is not uniformly successful. The inhalation of creosote from a nebulizer, operated by compressed air, should be equally effective, and would be much more pleasant and easily managed. This method was successfully adopted recently by Dr. W. Warner Jones in bronchiectasis following influenza in a man whom the writer referred to him for treatment.

Treatment by intratracheal injections has given satisfactory results. The following combination of remedies is frequently used:

| | |
|---|---|
| Menthol | 10 parts. |
| Guaiacol | 2 " |
| Olive oil | 88 " |

A dram of this is to be injected twice daily, care being taken to introduce the tip of the nozzle of the syringe beyond the vocal cords. Unfortunately it is not an easy matter to pass the nozzle of the syringe through the glottis without causing spasm, yet with average dexterity the injection should be made without much difficulty. This fluid often proves quite irritating and causes severe coughing. Iodoform emulsion, 2 to 10 per cent., is less irritating and is probably quite as effective.

Mendel[1] has improved on this method. He says that "if the tongue of the patient is protruded and held outside the mouth, and if he at the same time refrains from swallowing, the pharynx forms a funnel in which the inferior outlet is the glottis, as the orifice of the œsophageal tube is closed except during the act of swallowing, so that a small quantity of liquid projected against the wall of the pharynx runs down into the air passages." The liquid may be projected against the posterior wall of the pharynx, but it is more convenient and equally successful if the syringe is supported against the posterior faucial pillar and the fluid projected against the lateral pharyngeal wall, from which it runs around to the posterior wall and thence down through the larynx into the trachea. The tongue should be kept protruded a few seconds after the injection, so as to allow time for the fluid to flow through the larynx. He advises the use of non-irritating antiseptics, as eucalyptol, 5 to 10 per cent. The first injections should be very weak to allow time for the patient to become accustomed to them.

The essential oil in the fluid begins to evaporate as soon as it reaches the trachea and bronchi, and the vapor stimulates inspiration, causing greater expansion of the lungs. At first the increased expansion lasts only an hour or two, but the time gradually lengthens until the increased expansion becomes permanent. Mendel advises an injection of 3 cc. (45 minims) three

[1] *Lancet*, vol. ii. 1905. p. 133.

times daily for a month, to be resumed again as the patient's condition renders it advisable. The local effects are: (1) the cleansing of the larynx; (2) the lessening of the cough and bronchial secretion and the disinfection of the latter; (3) increasing the expansion of the lung so that there is better aëration of the blood. The treatment is easily carried out and should be effective. The *hypodermic injection* of guaiacol or creosote in sterilized oil, 1 part in 4, has been recommended, 30 minims (2 cc.) being given at each injection. Very little can be hoped for from such treatment.

The *direct injection* of similar solutions into the affected area of the lung has been attempted. If there were only one cavity and it could be definitely located, such a course might be attempted with some hope of success; but with a number of cavities filled with pus any effort at local disinfection by such injections must prove futile.

*Surgical treatment* has hitherto been too disastrous to render resort to operation advisable except in rare cases. The uncertainty of diagnosis, the infrequency of a single cavity, and the dangers from hemorrhage and other accidents have as yet prevented material advances being made in pulmonary surgery, but the future may bring better results. In cases with a single cavity that can be located, and with obliteration of the pleural cavity at the site for operation, free incision and drainage should give satisfactory results. Roswell Park has reported 23 cases of bronchiectasis operated on for drainage, with 9 deaths. He points out that in the absence of pleural adhesions the operation is difficult and dangerous; otherwise it is easy, especially if the cavity lies near the surface.

A dry climate, free from sudden changes, is most suitable for patients with profuse secretion. For the more robust the bracing, dry air of a northern climate, such as the Canadian Northwest, should be very beneficial; the debilitated will do better in a milder climate, such as that of Southern California, where they can spend many hours with comfort out-of-doors without much exertion or difficulty in keeping warm. In England, Bournemouth, and other places in the south are preferred. Upper Egypt affords probably the most desirable resort in winter, the air of the desert being very dry and not depressing. Unfortunately most persons affected are not able to bear the expense of such a course. Wherever they go these persons require special facilities, as the odor of their breath may render association with people impossible.

**Congenital Bronchiectasis.**—Bronchiectasis is occasionally found in the newborn. It is usually confined to one lung, but both may be affected. The lung is filled with cysts; usually the smaller bronchi contain serous fluid. They may communicate with the bronchi or form closed sacs. Sometimes a large, central cyst is found, with secondary or even tertiary cysts branching from it. Grawitz[1] describes such a case in which the right lower lobe was affected. There was a large, flaccid cyst, with thin walls lined by several layers of cuboidal epithelium, the superficial one being ciliated. Examination showed reasons for believing that it might have originated from hydrops of a main bronchus. A system of cavities separated by thin walls opened into a central one, and from the largest of these, secondary and even tertiary cysts arose so that numerous larger and smaller recesses were formed. Between the cyst and the healthy part

[1] *Virchow's Archiv*, vol. lxxxii, p. 217.

of the lung there was a boundary zone consisting of embryonal lung tissue, which appeared emphysematous. Goitre has been present in some cases. Reports of several cases of a somewhat similar nature have appeared in the literature.

Four cases of unilateral atrophy of the lung are described by E. Neisser;[1] they probably resulted from congenital bronchiectasis. In all the four cases, from earliest childhood there were intermittent attacks of cough, dyspnœa, attacks of fever, and putrid or bloody sputum. The health was fair in the intervals between the attacks. In all, atrophy of the left lung, compensatory hypertrophy of the right lung, displacement of the heart to the left, and a highly arched diaphragm were found; but there was no contraction of the left side of the thorax, which was regarded by Laennec as a constant condition in unilateral atrophy of a lung. The author, after a critical review of the literature of the condition, thinks all such cases are congenital, or acquired in earliest infancy, but admits the possibility of its occurrence in later life if it developed very slowly and thus afforded time for compensating hypertrophy of the right lung. Two of his cases occurred in father and son, and this, he thinks, shows a degree of hereditary influence. No reason is suggested to explain the affection of the left lung in all cases.

Ogle[2] reports a case of bronchiectasis in a man, aged twenty-eight years, who died from profuse hæmoptysis. Physical signs during life suggested empyema. The temperature was hectic and the sputum offensive, suggesting bronchiectasis. Postmortem, a cavity four inches in diameter was found in the right lower lobe near the surface. The cavity contained hair, a tooth, pultaceous material, and other substances characteristic of dermoid growth, and appeared to be a dilatation of the middle division of the main bronchus. The dermoid growth appeared to have originated in the mediastinum, invaded the lung, and caused a bronchiectasis by pressure on a bronchus, and then to have invaded the cavity thus formed, to whose walls it afterward became adherent. The patient had been ill with cough and hæmoptysis intermittently for five years.

*Atelectatic bronchiectasis of Heller* differs from the foregoing cases in the persistence of remnants of fœtal lung tissue that remains unpigmented and unexpanded; in the remarkable growth of cartilages in the bronchial walls, and in the fact that the epithelium is squamous and not ciliated. More recently cases with similar fœtal remains are reported as found in persons dying at an advanced age, in whom, however, finely granular pigment was found in the fœtal lung tissue, and in some, hypertrophy of the bronchial cartilages was wanting. In some of them there was deformity of the chest wall; the foramen ovale was found open in one case.

## BRONCHOSTENOSIS AND BRONCHIAL OBSTRUCTION.

**Etiology.**—Narrowing of a bronchus, even to complete obstruction, may occur in a great variety of acute and chronic affections. The cause may be situated without or within the tube, or in the bronchial wall itself.

[1] *Zeitsch. f. klin. Med.*, 1901, xlii, p. 88.
[2] *Transactions of the Pathological Society of London*, 1897, p. 37.

**Intrabronchial Causes.**—(1) Foreign bodies (discussed under that title), and (2) tumors or diseased glands which grow into or perforate a bronchus.

**Extrabronchial Causes.**—(1) Pressure from diseased and enlarged bronchial glands. The lymphatic glands lie chiefly at the lower end of the trachea and around the main bronchi, the largest being at the bifurcation. They receive the lymph from the bronchial lymphatics and arrest solid particles entering through the bronchial mucous membrane, as bacteria and dust. Large quantities of dust particles may mechanically increase the size of the glands to a considerable degree, but the chief causes of their enlargement are the toxins and bacteria of the various diseases in which the bronchi are involved. In the adult, pulmonary tuberculosis is the source of infection of the glands in the great majority of cases.

In children the lymphatic glands are normally large and very active, and therefore very liable to become infected, so that the bronchial glands may be greatly diseased, although the lungs are little, if at all, affected.

The bronchial glands may also become infected by malignant or tuberculous diseases of the abdominal organs. The infection may spread to the supraclavicular glands and cause their symmetrical enlargement. This bilateral affection becomes, therefore, a sign of much value in the diagnosis of abdominal and posterior mediastinal diseases. The enlargement of these glands may also occur following tuberculous disease of the cervical glands.

A. Fränkel draws attention to the fact that constriction of the bronchi may be occasionally caused by the pressure of an inflammatory mass resulting from peri-adenitis. The contraction of the cicatricial tissue produced may also compress the bronchus. In the latter case there may be stridor, contraction of the chest walls, weakened respiration, and dulness. In slowly developing cases the stridor and dyspnœa may be absent.

2. *Aneurisms* of the second part of the arch of the aorta are those most likely to press on the air tubes. They usually develop upward and backward and press at once on the trachea at its bifurcation. As the chest is shortest in all its diameters at the upper part, even small aneurisms may produce marked pressure. The symptoms of bronchostenosis may be the only indications of the condition until severe, even suddenly fatal, hemorrhage occurs. Similar symptoms may arise when the aneurism is of the innominate or the left carotid artery. Aneurism of the descending aorta may extend forward and compress the left bronchus.

3. *Mediastinal Tumor.*—The malignant forms are the most important, as by their continued growth they are certain, sooner or later, to press on the bronchial tubes. It is not, however, by pressure on the air tubes alone that they produce their symptoms. Dyspnœa may be caused by secondary deposits in the lungs, pressure upon large vessels, pleuritic effusion, bronchitis, and pneumonia, and by laryngeal spasm excited by pressure on nerves.

The diagnosis may be easy if the signs of a solid mass in the mediastinum are definite, such as dulness beneath and on each side of the sternum, and in the interscapular region. If the lung tissue over the mass is not completely airless there may be increased vocal fremitus and resonance with tubular breathing; fulness of the veins of the chest or of the neck, with, in many cases, œdema of the corresponding parts owing to pressure caused by obstruction to the return of the blood to the heart; pressure on arteries, as shown by a small pulse; pressure on the laryngeal nerves, causing paralysis

or spasm of the laryngeal muscles; and pressure on bronchi, obstructing the entrance of air into the lung.

4. *Abscess* in the mediastinum may be indistinguishable from tumor. It may arise from disease of the bronchial glands, sternum, vertebral column, clavicles, or œsophagus. The following case is a good illustration: A carpenter, aged forty-two, had catarrhal bronchitis, with dyspnœa, beginning in November. The cough was loud and clanging and the sputum frothy. There was the sensation of a valve-like obstruction in the trachea, which was relieved by lying on the left side, but greatly increased by lying on the back. There was rhonchial fremitus, with the increased respiration of exertion, most marked on the right side; coarse, piping rhonchi were audible in inspiration, and a wheeze in expiration. He had intervals of relief until the following February, when the dyspnœa grew much worse, the temperature began to rise, and the sputum became thick, tenacious, and greenish yellow. In a few days the dyspnœa and cyanosis became very marked and rales were abundant. An emetic was given, but the vomiting was followed by increasing distress for a few hours. The temperature rose to 102° and pulse to 120. A week later there was a profuse discharge of pus, and he died in a few hours. An autopsy was not permitted.

5. *Syphilitic infection* may involve the bronchial glands. In Hodgkin's disease and leukæmia the bronchial glands are frequently affected and often form enormous masses, which may compress the bronchi, especially in children.

6. *Pericardial effusion and dilatation of the left auricle* occasionally become so great as to compress one or both bronchi. Hypertrophy of the heart may possibly compress the left bronchus and the trachea.

*Stenosis due to disease of the bronchial wall itself occurs* most frequently in the smaller bronchi. Only those affections in which the stenosis causes the chief symptoms should be considered as cases of bronchostenosis. Among these is a disease first recognized during life by Fränkel, and which he described as *bronchiolitis acuta fibrosa obliterans*. It may be fatal in a fortnight. His attention was drawn to it by Lange's description of the post-mortem findings in two cases. The lungs were described as thickly studded with small, white nodules, as in acute miliary tuberculosis, and it was seen that the bronchioles were blocked with new connective tissue. Fränkel's first case was a man who had inhaled caustic vapor in large quantities, and was at once attacked with dyspnœa, which passed off after a time. Repeated attacks of dyspnœa followed. On admission to the hospital there was extreme difficulty in breathing, with cyanosis, and the lungs were greatly increased in volume. No distinct dulness was found, but everywhere small, vesicular sounds were to be heard; there was no fever. There was temporary relief as the acute inflammation following the necrosis of epithelium caused by the gas abated, but the dyspnœa recurred when the granulation tissue in the injured bronchiolar walls increased and narrowed the bronchioles, in many places even closing them. The autopsy proved the correctness of the diagnosis.

Other causes of stenosis are:

1. Ulcerations following traumatism, as burns, injuries by foreign bodies, etc.

2. (*a*) Syphilitic ulceration followed by cicatrical contraction; (*b*) syphilitic peribronchitis; (*c*) gummata in the walls of the larger bronchi.

3. Tumors of the bronchi.
4. Perichondritis.
5. *Bronchostenosis ecchondritica*, described by Gerhardt. In a case there was found marked thickening of many cartilaginous rings and covered by a layer of bone.
6. Spasm is believed to be a cause by some writers.

**Special Pathology.**—Besides the constrictions, bronchial dilatations exist above and below the point of constriction, the proximal widening being due to the inspiratory force, and the distal to the expiratory. Emphysema is common. If the obstruction is in a bronchial branch there may be atelectasis of the corresponding portion of the lung.

**Symptoms.**—The prodromal symptoms of stenosis of the respiratory tract vary with the condition on which it depends. The stenosis, as soon as it causes material obstruction, is characterized by the following symptoms: troublesome dry cough, occasionally with frothy sputum and streaks of blood; retrosternal pain or distress, usually definitely localized; voice hoarse and broken; constant dyspnœa, more or less severe, with paroxysms of extreme distress, and accompanied by two characteristic phenomena, viz., *coarse, noisy respiration* and *retraction of the chest.*

The *noisy respiration* in marked cases is audible at a considerable distance, and is increased on exertion; it is caused by the air passing through the constricted portion of the tube. It is loudest in inspiration, but occurs also in expiration. On auscultation it is usually loudest over the sternum, but may be most marked in the interscapular region. The loud, sonorous breathing of pharyngeal obstruction is distinguished by its disappearance on pinching the nostrils or closing the mouth.

*Retraction of the chest* occurs in inspiration and is apparent in the intercostal spaces, the suprasternal notch, the supraclavicular areas, and in the epigastrium. If the stenosis affects only one main bronchus, the retraction is limited to the intercostal spaces of the corresponding side.

A third symptom of importance is the *enfeeblement of the vesicular murmur*, the normal character being at the same time preserved. This phenomenon is observed over the area corresponding to the obstructed tube, so that it may be bilateral, unilateral, or limited to the part of a lung corresponding to a large bronchus.

The urgency of the dyspnœa will depend, first, on the suddenness of the development of the obstruction, and, secondly, on its degree. The sudden closure of a main bronchus causes great, even dangerous dyspnœa. The marked resulting disturbances of circulation tend to cause œdema in the unobstructed lung and may be quickly fatal. After the shock abates, as well as in cases of slowly forming contraction, even although marked, the dyspnœa may be slight, and material discomfort felt only on active exertion. In children it may resemble asthma and doubtless is often mistaken for it. In long-standing constriction, bronchiectasis in the affected lung is frequently developed. There may be atelectasis or emphysema, and often bronchopneumonia.

*Cough* is usually present in all well-marked cases of constriction. It may be paroxysmal and of a laryngeal character, or it may resemble whooping-cough. In many cases it is short and hacking. The cough varies according as it is excited by the catarrhal inflammation which always occurs at the seat of constriction, the reflex disturbance caused by the pressure

of the obstructing agent on the bronchus, or the direct irritation of the recurrent laryngeal or pneumogastric nerve. The last-named cause may affect the voice and also slow the action of the heart.

The sputum is often mucoid, especially in the early stages; later it may become muco-purulent or purulent. Tubercle bacilli may be found in it if a suppurating gland perforates a bronchus. *Hæmoptysis* is not infrequent, but is usually scant. It is probably due in most cases to congestion of the mucous membrane at the seat of constriction.

*Pain* is not uncommon, but rarely marked; it is usually referred to the upper dorsal region, but may also be felt behind the upper part of the sternum. In many patients there is a feeling of pressure deep in the chest. In malignant cases the pain may be severe. Emaciation and fever of a remittent type occur in children when the glands are extensively diseased.

*Physical examination* will give results varying according to the nature and seat of the obstruction. If a main bronchus is compressed, the expansion of the corresponding side of the chest will be lessened and the normal respiratory sounds feeble or lost, while in the opposite lung the sounds will be exaggerated, the chest increased in size, and the diaphragm lowered. The percussion note will be unaltered on the affected side if no complications in the lung have arisen. If the mass is in the posterior mediastinum there may be dulness in the interscapular region; if in the anterior, there will be dulness over and on either side of the upper end of the sternum. Often in partial occlusion of the bronchus a stridulous inspiratory sound is heard and the vibration may communicate a thrill that can be felt in the chest wall. Eustace Smith states that even in moderate enlargement of the glands at the bifurcation of the trachea a "hum" is audible over the first part of the sternum if the child throw the head well back. He believes the sound is due to pressure on the innominate vein by the enlarged glands which are carried forward by the trachea. The sign is much more rare in the adult. The glands may be so much enlarged as to press upon the œsophagus and cause difficulty in swallowing.

If tuberculous glands soften and form abscesses, they may rupture into the mediastinum and give rise to pyæmia and cerebral abscess; or into the pleura and cause empyema. A gland may perforate the trachea or a bronchus and be coughed up and ultimate recovery follow; more usually it causes suffocation, septic pneumonia, or pulmonary tuberculosis. If a gland perforates the aorta a rapidly fatal hemorrhage or embolism will result; if the pulmonary artery is perforated there will be pulmonary infarction or fatal hæmoptysis. A double perforation may occur, as into a bronchus and the pleura, causing pneumothorax, or into a bronchus and the mediastinum, causing emphysema.

**Diagnosis.**—Three principal signs—loud, sonorous breathing, retraction of the chest, and feeble vesicular sounds—are most characteristic. The only affection producing similar symptoms is laryngeal obstruction. In the latter the voice is much more altered and an examination of the larynx shows it to be the seat of the obstruction. Such an examination may demonstrate that the stenosis is tracheal. If the bronchoscope can be used it may show, not only the seat, but also the nature of the obstruction. Furthermore, in laryngeal constriction the larynx makes marked excursions in respiration, while in tracheal and bronchial obstruction it is immobile in breathing as well as in speaking.

The seat of the obstruction, if in the trachea, can be demonstrated by the respiratory sounds being equally affected in both lungs; besides, by the mirror and palpation the exact site may be determined. If the obstruction is in either main bronchus or in a large branch, the enfeebling of the respiration will be unilateral in the former case and limited to a lobe in the latter.

**Prognosis and Treatment.**—These depend wholly on the nature of the cause. In stenosis from syphilis and pressure by aneurism, large doses of potassium iodide may do much good, and even in cases of uncertain diagnosis the iodide may prove of much service. In the paroxysmal dyspnœa caused by the pressure of an aneurism, inhalation of chloroform, venesection, or hypodermics of morphine and atropine may give relief. In occasional cases of cicatricial stenosis, dilatation of the constriction may be tried by passing graduated sounds through a tracheotomy opening.

Chiari removed, by tracheotomy, a sarcoma from the trachea of a girl aged eleven years. De Brun resected eleven rings of the trachea in removing a tracheal cancer. The result was satisfactory for five years; death occurred in the sixth year on account of recurrence.

## BRONCHIAL CALCULI (BRONCHOLITHS).

The term *bronchopulmonary lithiasis* is applied to the occurrence of stony concretions in the respiratory passages and organs—the *calcareous phthisis* of Bayle. The calculi may be formed in the bronchi, lungs, pleuræ, or lymphatic glands, and may consist of cartilaginous, bony, or calcareous substance. Bronchial lithiasis is usually a latent condition, calculi being frequently unexpectedly found at autopsy, especially in chronic tuberculosis; but calculi may be formed in other diseases and give rise to symptoms of irritation that simulate tuberculosis.

Clinically, the affection seldom shows signs of its existence except in the expectoration of calculi; this is of rare occurrence, but was known to ancient writers. Boerhaave described the case of the botanist Vaillant, who expectorated four hundred calculi. In general the number expectorated does not exceed one or two. The stones may be cartilaginous, osseous, or calcareous, and the cartilaginous calculi may originate from the tracheal or bronchial cartilages, being set free by ulceration; or from enchondroses of the tracheobronchial cartilages of inflammatory origin (Virchow); or from chondromata of the lung. These calculi have the appearance of cartilage and they can only be differentiated by microscopic examination from cartilaginiform masses of fibrous tissue, which may be set free from tuberculous lung by ulcerative processes.

*Osseous calculi* are distinguished from the calcareous by their microscopic structure showing the presence of osteoblasts and Haversian canals, as in true bony tissue. They may originate from the *bronchial cartilages*, ossification following inflammation of long duration, as in bronchiectasis and pulmonary phthisis; from *pleural ossifications* occurring in old pleurisies; from *pulmonary ossifications* which form in the walls of old abscesses; in tuberculous and non-tuberculous scleroses and in true osteomata, and, very rarely, in the *tracheobronchial mucous membrane*, the seat of old disease.

*Calcareous stones* are due to the calcification of various tissues of the respiratory organs and to the incrustation of exudates by the deposit of granules

of tribasic phosphate of lime and carbonate of lime, without any tendency to ossification. The calcifications in the respiratory organs may be parenchymatous or form in cavities.

In the first group are: calcifications of the tracheobronchial cartilages, as observed in aged persons; calcifications of tuberculous bronchial glands; calcifications in the lung, which may be healthy or previously diseased; calcifications of various tumors; calcifications of the pleura following purulent exudates. In the second class: free concretions in preëxisting cavities and in inflamed dilated bronchi or in pathological cavities of the lung, especially in those of tuberculous origin. These concretions result from the incrustation of stagnant, muco-purulent secretions. They may also be found in the bronchi, around a foreign body of any kind.

## FOREIGN BODIES IN THE BRONCHI.

Under this heading are included only substances in masses of various sizes, and not particles of solids like dust or fluid substances, as blood or pus, although they too are foreign substances.

It is not rare for various kinds of foreign bodies to reach the bronchi by way of the respiratory passages. The accident occurs most frequently in children, but adults also furnish a large contingent. It is a matter for surprise, not that the accident occurs so frequently, but that it is not of much more common occurrence, owing to the fact that anything held in the mouth may, by an accidental reflex inspiration, be drawn into the trachea and thence into the bronchi. In view of the danger the objectionable habit that is so general, of making the mouth a receptacle for holding pins, needles, buttons, seeds, etc., cannot be too strongly condemned. The accident is most apt to occur while a person is intently occupied in some study or difficulty during which the sentinel muscles of the larynx are resting and off guard. Under such conditions the sudden deep inspiration preceding a laugh or cough, or a strong effort, while the glottis is widely dilated, offers a favorable opportunity for the entrance of the foreign body. During vomiting, some of the ejected contents of the stomach are liable to be drawn into the trachea by the deep inspiration that immediately follows the act of expulsion. The danger is greatly increased by narcosis from any cause.

The danger is greater still during anæsthesia, during which the sensitiveness and reflex irritability of the glottis are lessened, as shown by the frequency with which teeth extracted under anæsthesia have fallen through the open glottis into the trachea. Pieces of excised tonsil, uvula, polypus, and small instruments used in operating in the mouth, have also fallen or been inhaled into the trachea.

In the coma of all intoxications, in all paralytic affections, local or general, involving the larynx, in local diseases of the glottis, as tuberculous and malignant ulceration, and even in natural sleep, the efficacy of the glottic guard is diminished and the liability to the accident therefore increased.

In a group of rare cases the foreign body gains access to the respiratory passage through openings below the glottis, as a tracheotomy wound, a bullet or stab wound, or by ulceration into the trachea of a caseous or calcareous gland. A foreign body in the œsophagus, as a fish-bone, may find its way slowly into the trachea. Pibray, Henry the Fourth's surgeon,

recorded the remarkable case of a man coughing up about three inches of his own rib (West).

As a rule the foreign body is carried, as soon as it passes the glottis, to as small a bronchus as can receive it. Not rarely, however, the body lodges for a time in a bronchus of larger size, and is found to descend gradually to a smaller one, requiring some days to reach and become impacted in the smallest tube it can enter. During this time it may be shifted by the cough from place to place in the tube, or moved into other tubes; in these excursions it may be carried up into the trachea and thence drawn into the other lung. This occurred recently in a lad with a bullet in his bronchus, whose case will be referred to later, and shows that even heavy bodies may be shifted about by the force of expiration in coughing. Lighter bodies, such as large seeds, may be kept moving back and forth for several days, especially if they strike on the spur at the bifurcation of the trachea, or the spur of a bronchus formed by the giving off of a branch.

Foreign bodies pass more frequently into the right than the left bronchus for the following reasons: first, the right bronchus is more nearly vertical and therefore more in the course of the trachea than the left; secondly, the interbronchial septum extends upward from the bifurcation of the trachea toward the left side, so that the foreign body is directed toward the right bronchus; thirdly, the right lung and right bronchus are of larger size, and consequently the aspiration power of the right lung is greater than that of the left. However, the difference in the frequency with which bodies enter the two bronchi is probably not so great as is generally supposed. Statistics are of little value, owing to the defects in the observations and descriptions of cases, and therefore scarcely afford any assistance in a given case.

The position of the patient probably has much to do in determining the course of the foreign body. Thus, if the patient's body is inclined to the left the trachea will be thrown still more into line with the course of the right bronchus, and vice versa.

**Special Pathology and Sequelæ.**—The morbid changes depend on various circumstances, as the length of time the foreign body lodges in the bronchi, whether its surface is smooth or uneven, and, chiefly, whether it is aseptic or carries with it septic organisms.

As a rule, if the foreign body be got rid of in a short time, the bronchial irritation excited by its presence soon disappears and no trace is left of the injury; but if it remains long lodged in a bronchus morbid changes are almost certain to result, either at the seat of impaction or in the lung beyond it. The chief danger, however, is not usually from the body itself, whatever its size or form, but from the septic organisms that are carried in with it. This danger will vary according to their number and virulence, and the vital resistance of the tissue of the bronchial wall which they infect. Particles of pure food may be practically harmless in the bronchi and alveoli, being rapidly absorbed, causing at most only a simple catarrh which passes away completely after a few weeks. In the case of larger bodies, however, lodging more than two or three days, chronic inflammation as a rule results. The inflammation in addition to the bronchitis may extend to the deeper parts of the bronchial wall and to the adjacent lung tissue, and lead to more or less extensive fibrosis. This cirrhotic change may extend to the whole of the lung, corresponding to the occluded bronchus.

Unfortunately, in the great majority of cases septic changes of greater or

less severity occur. The microörganisms may be introduced with the foreign body, or, if this be aseptic, the bacteria normally present on the surface of the bronchial mucous membrane may excite local septic changes after the epithelium has been injured or destroyed by the foreign body. If the body be friable it may break up and the parts be carried to other parts of the lung, causing septic infection wherever they lodge. The septic inflammation in many cases is confined to the bronchial wall, but in a large number septic pneumonia is set up, resulting in local suppuration or gangrene. In these cases the result depends on the virulence and number of invading microörganisms and the vital resistance of the tissues involved. Frequently only a local abscess is formed which may rupture into a bronchus and the contents, including the foreign body, be coughed up. In such a case the cavity may cicatrize after a time, during which it discharges a gradually diminishing secretion.

In other cases the infection is less virulent and gives rise to a more chronic inflammation, which may produce much interstitial change in the lung. In this manner the whole of the affected portion of lung may become densely fibrosed, with more or less dilatation of its bronchi. More frequently irregular cavities form in it, either from dilated bronchi in which much ulceration has occurred, so that they resemble tuberculous cavities, but they can be demonstrated to be non-tuberculous, and only due to local destruction of pulmonary tissue. If much lung is involved the corresponding part of the chest becomes contracted, in some cases to a marked degree. Such marked changes rarely affect more than a portion of one lung, although cases are on record of a whole lung being involved from obstruction of the main bronchus.

*Bronchiectasis* develops in not a few cases, and is due to a variety of causes. It is especially apt to be produced in cases in which there is only partial occlusion of the bronchus. The air can enter the lung beyond the obstruction, but the catarrhal secretion, being disturbed by the cough, often narrows still further, or even completely closes the obstructed bronchus so that the air cannot escape. The next inspiration expands the affected lung, and the entering air, forcing back the mucous obstruction, fills it; with expiration, which is so often accompanied by the force of cough, the secretion is again driven into and occludes the narrowed outlet. The pressure of the pent-up air in time dilates the bronchi, the walls of which have by this time been injured by the inflammation that has extended throughout their length.

When suppuration takes place around an impacted body, it may be found lying loose in the abscess cavity. The abscess may rupture into the pleura, and the body then may lie loose in the empyematous cavity. Such accidents may occur after many years of impaction, during which symptoms were quiescent. In Carpenter's case false teeth were found in the cavity of an empyema at autopsy, thirteen years after they had disappeared down the patient's throat.

**Symptoms.**—In most cases the entrance of a foreign body through the glottis into the trachea is attended by alarming symptoms of dyspnœa, even of strangulation, owing in part to laryngeal spasm and in part to mechanical obstruction. But, in a large minority of cases these symptoms are not extreme; in children they may be so mild as not to attract attention until the body causes dyspnœa by obstructing a large bronchus, or by its movements excites reflex laryngeal spasm. Much will depend on the size, shape, and character of the body, a smooth one causing less disturbance than an

angular or pointed one. A large body lodging at the tracheal bifurcation may quickly cause death from suffocation, while a small one, if it passes on in a small bronchus, may produce little, if any, immediate disturbance.

The dyspnœa is usually inspiratory, like that of laryngeal obstruction, if severe, being marked by inspiratory recession of the soft parts of the chest and of the epigastrium, and of the lower ribs in children. In the beginning of the attack dyspnœa is, as a rule, chiefly due to the laryngeal spasm. This may be excited by even a very small body. The spasm usually passes off soon, unless fresh attacks are induced reflexly by movements of the body in the trachea and bronchi, and any persistent dyspnœa that may occur will be caused by the mechanical obstruction to the passage of air. However, the fact should not be overlooked that the foreign body in its passage may injure the larynx and the resulting inflammation after a few hours may cause a gradually increasing dyspnœa which may become extreme. Cyanosis is present in proportion to the degree of obstruction. While the dyspnœa is as a rule inspiratory, it is in some cases expressly stated to have been expiratory. This persistent dyspnœa is in some cases marked by occasional exacerbations so as to simulate bronchial asthma; in these the foreign body is evidently movable. It is quite conceivable that, in susceptible persons, a genuine asthma may arise from such an irritant.

If the body is driven against the glottis during the expiratory efforts of coughing, or even strongly irritates the region of the septum at the tracheal bifurcation, the attacks of suffocation may be so severe as to threaten life. The patient gasps for breath, the face becomes livid, the eyes prominent and staring, the veins distended, the heart tumultuous, and a copious perspiration may be poured out. Foam, often mixed with blood, may form in the mouth and nose, and the patient may be thrown into a frenzy of distress or become quite unconscious.

The *physical signs* vary according to the seat and degree of obstruction. If the body is large and lodged in the trachea it will influence the respiration in both lungs, altering the normal breath sounds, lessening expansion of the chest, and producing stridulous inspiratory and possibly expiratory sounds.

If the foreign body passes into a bronchus and completely occludes it, there will be complete loss of breath and voice sounds over the lung, or part of it, supplied by the occluded bronchus; but if the occlusion is only partial a stridulous or piping rhonchus that is persistent may be heard; if the occlusion is slight or occurs in a small bronchus, the alteration of the normal signs may be slight or even unrecognizable. If a large bronchus is completely closed, the lung may collapse and contraction of the corresponding part of the thorax follow. But instead of collapse the lung may become consolidated from the occurrence of pneumonia, even within a day after the entrance of the foreign body. In such a case, all communication with the external air being cut off and the bronchi soon filling with exudation, there will be loss of all respiratory sounds.

If only atelectasis occurs, the bronchi being full of air, the signs of consolidation will not be complete. The percussion sound will depend on the amount of air in the bronchi. If the obstruction of the bronchus is complete, all respiratory sounds should be lost as well as movements of the chest. If the occlusion of the bronchus by the foreign body is partial, the normal respiratory sounds may be only weakened, the lessening of the sounds being in proportion to the degree of impediment to the entrance of air.

Sonorous and sibilant rales may be produced as soon as bronchitis occurs around the foreign body, and their existence will be of much diagnostic importance. The rales may be very loud, and sometimes cause a thrill which may be transmitted to the trachea.

If the foreign body be movable it may excite paroxysms of dyspnœa and cough as its position is shifted, especially from one bronchus to another; it may even be transferred to the opposite lung. If it is small, these movements may lead to its being carried down into a small bronchus, with complete relief of all symptoms until local inflammation is excited. This sudden relief to dyspnœa and cough may lead to the belief that the body has been expelled, and it may require some time to determine whether such is the case, or that it has become lodged in a small bronchus. While dyspnœa and paroxysmal cough are present in nearly all these cases, yet in occasional ones there is remarkable tolerance of irritation, and nearly all symptoms may be absent.

The sputum is usually catarrhal at first, but it may be mixed with a small quantity of blood. If the body be angular and sharp, or has remained long in the same place and caused the erosion of a large vessel, bleeding may be profuse and even fatal.

The position assumed by the patient may affect the symptoms, especially if the body be movable. Naturally he assumes the position in which the foreign body is least disturbed.

**Diagnosis.**—If a clear history is obtained and the symptoms are typical, the diagnosis is easy; otherwise, it may present the greatest difficulties. In recent years the *x*-rays have afforded valuable aid, in some cases not only proving the presence of the body, but also its exact location. If there be urgent dyspnœa this may not be practicable. The bronchoscope is the most recent addition to the appliances for examining the interior of the respiratory passages.

In young children the differentiation from laryngismus stridulus may be difficult; and from whooping-cough, or even from asthma if the spasm occurs, it requires care. If laryngitis is excited, the symptoms of the inflammatory condition may mask those of the foreign body. The most difficult cases are those in which there is no history of the entrance of a foreign body. These cases often present the most anomalous symptoms. In all cases, especially children, with such unusual symptoms, more than half the difficulty may be overcome by bearing in mind the possibility of a foreign body. This cause should be present to the mind in all cases showing signs of local septic pneumonia, or gangrene of the lung, or of general pyæmia with signs of early involvement of the lungs.

**Prognosis.**—In the early stage the dangers to life are very great from sudden suffocation or from spasm caused by the body being coughed up against the larynx; in the later stages the danger is from septic changes liable to occur around and beyond the impacted body. In 89 cases of foreign bodies in the air passages reported in the literature, Wood[1] found gangrene in 9 per cent., with deaths in 75 per cent. of these; abscess in 29 per cent., death resulting in all with multiple abscess, and in 30 per cent. of those with single abscess; pneumonia in 11 per cent., and death in 40 per cent.; and bronchitis in 18 per cent., with a mortality of 6.25 per cent.

Although the outlook generally is so bad when the body is not early

[1] *Philadelphia Medical Journal*, 1899.

expelled or removed, there are cases in which it has remained impacted for years and was then spontaneously expelled or removed, perfect recovery following. Burch and Lake[1] report a case in which a piece of bone was removed from the trachea after being embedded there for nine years; recovery followed. They also give a table of the cases recorded during the last century—31 in all—in which the body had been for a year or more in the lower air passages. In those terminating fatally the cause of death was almost always tuberculosis.

The prognosis varies considerably with the physical character of the foreign body. Hard, smooth ones are less likely to become lodged and are more easily expectorated than are the hard, irregular ones. Besides being more likely to become fixed the latter are also more difficult to remove. Fruit seeds are still more unfavorable in prognosis, especially those that swell in water. Heads of grain are rarely expelled spontaneously, they are probably difficult to remove even with the aid of the bronchoscope.

**Treatment.**—The first object in most cases is to get rid of the foreign body. In some the body is expelled spontaneously by coughing. To aid in the expulsion, emetics have been given to dislodge the body and permit of its being coughed up. During the straining and vomiting the head is placed below the level of the body so that gravity may favor the falling of the foreign body toward the glottis. Children have been held up by the legs and shaken, or slapped between the shoulders. These proceedings are not without grave risk, as the body by being suddenly impinged against the glottis may cause its spasmodic closure, with danger of suffocation. To obviate this danger tracheotomy is usually advisable, and that too as promptly as possible, as the conditions for operation are never more favorable than at once after the entrance of the foreign body and before any damage is done to the respiratory mucous membrane; the longer it is delayed the less favorable the conditions for it usually become. If the body is lying loose in the trachea or one of the larger bronchi, the cough excited by the tracheotomy often causes its prompt expulsion. This was the experience in an unpublished case of a boy aged ten, through whose glottis a bean had entered three days before the writer saw him. The bean was moving freely to and fro in the trachea and bronchi, causing paroxysms of dyspnœa from time to time. It was expelled immediately on opening the trachea.

The bronchoscope has proven of great service both in locating and in aiding the removal in cases in which the foreign body has not been expelled by coughing or vomiting. The efficiency of the instrument is well shown in the following case of a boy aged seven, whom the writer had seen with his physician, W. J. Wagner of Toronto. The boy said that he had swallowed a bullet or cartridge of a small revolver. It had at the time caused slight symptoms of strangulation, with cough, but they soon passed away. On examination some hours later, there was no disturbance except some shortness of breath, which became marked on exertion. After a few days signs of bronchial irritation were observed, and he soon became very ill, with signs of pneumonia and pleural effusion at the right base. He improved in about ten days and the temperature became normal, but the cough remained troublesome. The temperature rose again after a few days and the cough occurred in severe paroxysms. Over the right side the breath sounds had remained

[1] *Lancet*, September 25, 1897.

weak after the pleural exudate occurred. A few days later pain began in the left side, and over the lower lobe of the left lung the respiratory sounds were barely audible, while in part of the left lung as well as throughout the right there were numerous rales of great variety. The expectoration was swallowed. At this time an *x*-ray examination was made and the bullet shown to be lodged in a large left bronchus. Tracheotomy was performed by G. R. McDonagh and (by the aid of the bronchoscope) the bullet extracted with much difficulty from apparently the tertiary division of the bronchus.

Judging by the character of the cough and the expectoration occasionally ejected in the strangulation of some of the paroxysms, there seemed to be considerable bronchiectasis in both lungs. After the removal of the bullet the recovery was rapid and in a few months cough ceased and the boy's health was restored. It is remarkable that such a heavy, oblong body should have been dislodged from the right lung to the left by the force of expiration in coughing.

The early use of the bronchoscope, before the foreign body is carried down into the smaller bronchi, should be so generally successful that few cases should go unrelieved. The unsuccessful cases should be carefully watched so that if the body become dislodged by suppuration or otherwise a prompt effort may be made to remove it by the aid of the bronchoscope. Prolonged instrumentation should, however, be avoided, as it favors the development of pneumonia. Operation has been suggested for the cases in which the foregoing means fail, but the dangers and difficulties of opening the pleura and penetrating the lung are so great that it is seldom advisable. An expectant plan of treatment will probably give the best results.

## ASTHMA.

**Definition.**—The pathology of asthma is so imperfectly understood that it is impossible to give a satisfactory definition of the disease. All are agreed that a neurosis is an important factor, but many believe that there is also an inflammatory affection of the bronchioles, either as a primary lesion or at least as an important secondary condition.

*Pathologically*, the affection is characterized by a spasm of the bronchi and of the respiratory muscles, including the diaphragm, and by vasomotor disturbances of the bronchial mucous membrane. *Clinically*, the disease presents three fundamental symptoms:

1. The *paroxysmal character of the attacks:* these recur at variable intervals; they may even be periodical like those of migraine or epilepsy.
2. The *dyspnœa:* it is characteristic in that it is chiefly expiratory.
3. The *vasosecretory disturbance:* all the respiratory mucous membranes throughout become suddenly the seat of an abundant secretion; the mucous membrane of bronchioles, bronchi, trachea, larynx, nasal fossæ, and even the mucous membrane of the nasal duct and conjunctiva participate in this sudden hypersecretion. The secretion of the bronchioles demands chief consideration because of its exceptional viscosity, the nature of the cellular and crystalline elements which it contains, and because of the important part it plays in the mechanism of the paroxysmal dyspnœa.

In addition to these more marked symptoms there are also distention of the chest and depression of the diaphragm.

**Etiology.**—The essential nature of the malady being unknown, it follows that its fundamental cause must also be in doubt. In view of the fact that it is in the first place a neurosis, the cause must affect the respiratory centre, but the exact nature of the disturbance of this centre we do not know.

**Predisposing Causes.**—The predisposition to the disease, or more correctly the condition, whether hereditary or acquired, that renders the patient least able to resist the exciting agencies, is the cause of chief importance in essential asthma. Hereditary predisposition is sometimes direct from parent to child, the affection often appearing at the same age in both, and not rarely disappearing at the same age. It may run thus through several generations. It may avoid the direct line and appear in the collateral branches. Sometimes it appears in several members of one family without there being evidence of heredity. Many cases occur in families that are subject to other hereditary affections, as migraine, epilepsy, and gout. Males are said to be more frequently affected than females, the proportion being about two to one, but the statistics are questionable. The increased frequency of the affection in the male is probably confined to later life, when bronchitis is of more frequent occurrence, and possibly when gout has some influence. The poor are regarded as less often affected than the well-to-do, probably because they are less liable to gouty and lithæmic conditions.

*Diseases of the respiratory mucous membrane,* especially catarrhal conditions of the nasal passages, are of frequent occurrence before the development of asthma. All kinds of cutaneous diseases have been said to render their subjects liable to asthma, however with little, if any, good grounds. To neurasthenia and many other affections influence has been attributed, but with little reason.

*Age.*—No age is exempt, not even infancy. Probably the majority of cases begin in the early years of life. In 225 cases tabulated by Salter 31 per cent. began before the age of ten years. Few cases of uncomplicated spasmodic asthma begin after fifty, but the affection not rarely develops after that age in persons subject to bronchitis—that is, in early life asthma is generally a neurosis occurring without previous local disease, or independently of it if such exists, while as age advances it is more and more frequently preceded by and dependent upon changes in the respiratory tract. In little children it often disappears after a few attacks and in older children at the time of puberty.

**Exciting Causes.**—Asthma in the majority of cases is probably due to irritation of the terminals of the nerves in the respiratory mucous membrane by one or more of the many substances suspended in the atmosphere. This view is supported by the effect of many substances, as vapors, pollen of flowers, and emanations from animals, on certain persons, and by the occurrence of asthma in susceptible persons in certain localities only.

*Climate* and *seasons* have a very uncertain influence. The malady is probably more frequent from spring to autumn, but this may be due to the greater prevalence of such exciting causes as dust, pollen of grasses and flowers, etc., during this portion of the year. There is also the greatest capriciousness in regard to locality, probably for the same reason. Some patients are better in dry and others in moist places. Many are free in cities and afflicted in the country; or they may even find relief in one part of a city after being affected in another part only a short distance removed.

*Affections of the respiratory mucous membrane* exist in the great majority of cases, and the paroxysms are probably excited by irr.tation of the abnormal membrane or some part of it. This is especially true in regard to the nasal mucous membrane in which a certain point may be so sensitive that even touching it may bring on an attack. It is due to this fact that climate and locality have in many cases such influence on the occurrence of the attacks. The nasal mucous membrane when the seat of polypi and thickening from chronic catarrh, and the bronchial mucous membrane when affected by chronic inflammation, are the most important avenues through which the causes that excite the paroxysms act.

*Disease of the lungs* probably never causes asthma. During acute affections of these organs and of the pleura, in persons subject to asthma, the paroxysms usually disappear for the time being, to return again after recovery. Tuberculous patients rarely suffer from essential asthma, and asthmatic patients seldom become tuberculous, but when they do the asthma usually disappears. Dyspnœa is of frequent occurrence in pulmonary disease, but it is due to a variety of causes other than asthma, as sudden cardiac failure, acute pulmonary œdema, and pulmonary infarct. In affections of the heart true asthma is very rare.

Similarly, in *affections of the kidneys*, paroxysms of dyspnœa are also not uncommon and are due to similar disturbances of the circulation or to uræmia, but in these affections true asthma rarely occurs.

*Gout* as a cause of asthma was first pointed out by Trousseau. He records two cases; in one, a boy, asthma began at the age of five and gout occurred two years later. In the second the asthma was of long standing and gout began at twenty-one years of age.

*Functional disturbances of the stomach* are apparently the exciting causes in some persons; also those of the intestines, such as flatulence and constipation; relief from these affections may prevent further attacks. Irritation of the ear, of dentition, of the skin, and of the genital tract are also assigned as causes. Paroxysms have also been attributed to intestinal worms. Occasional cases have been met with in which the attacks occurred only during *pregnancy*, and in a few of these cases the disease became permanent toward the end of the childbearing period.

There are many cases for which we are unable to assign any cause. In some the respiratory centre is so unstable that slight departures from the daily routine may precipitate an attack. Travel may do so, and Fowler mentions the change incident to the rest over Sunday being sufficient to cause such disturbances in digestion and excretion as to be followed by an attack on Monday.

*Psychical impressions* may be sufficient to excite a paroxysm in neurotic persons. A lady in whom the fragrance of the rose always excited an asthmatic attack was handed one by her physician to test its effect; she took it under protest. A paroxysm immediately followed, although the rose was only an artificial one.

It seems therefore that in very susceptible individuals a peripheral irritation in any part of the body may be sufficient to excite a paroxysm. In the great majority of cases, however, paroxysms are only excited by irritation of some part of the respiratory mucous membrane.

**Special Pathology.**—This is a vexed question and cannot be considered in detail in the limits of this article. The general agreement that asthma is

at least largely a disease of functional nervous origin indicates that it presents no distinctive morbid changes. Lesions occur in various organs, but no constant change is found and those met with are usually secondary. All chronic cases show various secondary changes of which bronchitis and emphysema are the most frequent.

The essentially neurotic character of asthma is shown by its occurrence in paroxysms, but the greatest uncertainty has existed as to the means by which the paroxysms are excited. Various theories have been advanced to account for them. Of these theories the most important are:

1. That which attributes the paroxysm to spasm of the circular muscular fibers of the bronchial wall. This theory was first advanced by Williams and is probably the most widely accepted.

2. That which attributes it to swelling of the mucous membrane of the bronchioles from congestion either of vasomotor or inflammatory origin—fluxionary hyperæmia (Traube), swelling analogous to urticaria (Clark), vasomotor turgescence (Weber), *bronchiolitis exudativa* (Curschmann).

3. That the paroxysm is due to spasm of the diaphragm, or of the inspiratory muscles, or of both.

Other theories, such as paralysis of the bronchial muscles, with consequent loss of expiratory power (Walshe), and spasm of arterioles and œdema of the bronchial mucous membrane are now scarcely regarded by anyone as possibly correct.

1. In regard to the theory that asthma is due to bronchial spasm, it has been shown that the muscular coat of the small bronchi consists of two interwoven muscular layers, a thick one of circular fibers and a thin, longitudinal one. Under normal conditions the latter is able to prevent narrowing of the lumen of the tube, but if spasm of the circular fibers occurs, the resistance of the longitudinal fibers is overcome by the contraction of the thicker and stronger circular layer and narrowing of the caliber of the bronchus is the consequence. As spasm is never uniform, the narrowing is always irregular.

The effectiveness of bronchial spasm in producing the complete symptom-complex of a typical attack of asthma has been fully demonstrated by the experiments of Brodie and Dixon.[1] They point out that it has been thoroughly established that the vagus is the only motor nerve to the bronchial muscles, and that in the nerve run two sets of fibers, the constrictor and the dilator. Examination of the sympathetic gave negative results so far as the bronchial muscles were concerned.

Stimulation of the constrictor fibers of the vagus could be excited by muscarine, pilocarpine, and electric irritation of the nerve itself or of the respiratory mucous membrane, especially of the upper posterior surface of the nasal fossæ. The stimulation by any of these agencies always resulted in the production of all the signs and symptoms of spasmodic asthma. In all these cases the dyspnœa and distended thorax are of the typical character, and the sibilant rales are heard on auscultation. There is practically no engorgement of the lungs nor excessive secretion in the bronchi or bronchioles. Furthermore, the attack is at once arrested by subcutaneous injection of atropine, also by electric stimulation of the vagus, and that too without disturbing either the heart or the vascular system.

In accounting for the overdistention of the chest they point out that the

[1] *Transactions of the Pathological Society of London*, vol. liv, p. 38.

force of inspiration is much greater than that of expiration, and further, that the *inspiratory act* is violent while the expiratory is quiet and prolonged. The whole endeavor of the patient is to get more air into the lungs, while he is little concerned to drive it out. The exaggerated inspiratory act is required to cause the air to pass through the narrowed bronchioles into the alveoli. The expiratory act, being weaker and acting at growing disadvantage as the chest becomes increasingly distended, and as the depressed fixed diaphragm interferes with action of the abdominal muscles, is unable to empty the alveoli and equalize the ingress and egress of air. Besides, violent expiratory effort would probably further narrow the caliber of the bronchioles by compression, and thus increase the obstruction to the egress of the pent-up alveolar air.

Further evidence in favor of the theory of bronchial spasm is afforded by the sudden onset of an attack in uncomplicated cases and its almost equally sudden cessation. This is the usual course of events in spasm of involuntary muscular fiber, if there are no conditions developed which prevent the complete arrest of the irritation that excites the spasm. In the more chronic cases of asthma, the existence of bronchitis usually alters the typical course of a paroxysm so that the onset becomes less sudden and the termination more gradual and protracted.

2. There is much to be said in favor of the second theory which attributes the paroxysms to congestive swelling of the mucous membrane of the bronchioles and in many cases to exudation into their cavity. Turgescence of the bronchial mucous membrane from vasomotor paresis has been considered by many as analogous to that of the nasal lining, but the structure of the two membranes differs widely. The nasal mucous membrane, especially over the turbinated bones and lower nasal passages, is extremely vascular, and contains large venous plexuses surrounded by muscular fibers forming a kind of erectile tissue (Klein), while that of the bronchi is thin, and its blood supply relatively very scant. Yet the asthma-like dyspnœa occurring in capillary bronchitis proves that swelling of the mucous membrane of the smaller bronchi, either from vasomotor paresis or from inflammation, is sufficient to produce the mechanical condition necessary to induce paroxysms like those of spasmodic asthma. The occurrence of secretion in all but brief paroxysms proves that the membrane becomes at least congested. It is probable that there is only congestion from vasomotor paresis in the less protracted paroxysms, at least in the early period of the affection. The white spirals found in the sputum consist of dense mucus and contain no inflammatory products, showing that they are the product of congestion and not of inflammation. In a fatal case the epithelial lining of the bronchioles was found quite intact and the lumen of the tubes was filled with mucus (Schmidt). This does not prove, however, that the swelling of the bronchial mucous membrane and the secretion of mucus are the result and not the cause of the spasm of the small bronchi. Sooner or later bronchitis develops in all cases of asthma and probably renders the bronchial mucous membrane more susceptible to irritation. The condition becomes then an important predisposing cause of asthma. Further support is lent to this theory of urticarial swelling of the lining membrane of the bronchioles by the fact that there is great increase in the number of eosinophiles in the blood in both urticaria and asthma.

3. Spasm of the diaphragm and inspiratory muscles as a cause of asthma

may be dismissed as quite untenable. The distention of the chest and the spasm of all these muscles are the result, not the cause, of the paroxysm, during which the ingress of air under the greater force of inspiration is in excess of the egress under the lesser force of expiration, so that the chest gradually becomes more and more distended and the diaphragm depressed. The spasm and depression of the diaphragm cause distention of the abdomen and spasm of its recti muscles. This practically paralyzes the abdominal wall, thus destroying the most important agent in forced expiration.

Therefore, the conclusion seems justified that in asthma there is a neurosis which renders it possible for an irritation of a peripheral nerve, generally in some part of the respiratory tract, to be reflected through the vagus to the muscular wall of the small bronchi, causing spasmodic contraction of the tubes and possibly sometimes also, through the vasomotor system, producing hyperæmia and swelling of the mucous membrane of the bronchi, generally, if not always, secondary to the bronchial spasm.

Several varieties of asthma have been described according to the region or organ from which the reflex influences exciting the paroxysms emanate, as bronchial, nasal, renal, cardiac, etc. Numerous cases remain in which the origin of the reflex irritation cannot be determined. In this it resembles epilepsy and migraine, in depending upon an abnormal condition of the central nervous system either inherited or acquired. Finally, it may show itself as irritability of the general mucous surface of the respiratory tract, or of certain diseased areas of it, or as a part of general neurasthenia.

**Symptoms.**—The disease rarely begins suddenly, but in most cases is preceded by a longer or shorter period during which the patient is subject to bronchitic attacks, often with an undue degree of dyspnœa. In time the affection develops, the paroxysms being usually preceded by prodromal symptoms which the patient himself soon recognizes as indicating the approach of an attack. These symptoms vary widely; they may consist of general discomfort, of general buoyancy and vigor, of drowsiness and depression, of epigastric discomfort, of frequent yawning and coryza, with a good deal of secretion and sneezing or itching of the nose, or there may be only a peculiar taste to the saliva, and epigastric oppression without disturbance of digestion or loss of appetite. Whatever the symptoms may be, however, they usually continue of the same nature throughout the history of the case, like an epileptic aura, and always serve as a warning of a threatened attack; they may make it possible to ward off the paroxysm. Many patients are prone to bronchitic attacks on even slight exposure.

The paroxysms may occur at any hour of the day or night, but oftenest about midnight or later. Trousseau said that in his own case the attacks began as the clock struck three in the morning. A late meal often provokes a paroxysm in asthmatics, necessitating their denying themselves this luxury. The patient may go to bed comfortable, and awaken with the attack upon him. It usually begins with a sense of constriction in the throat or around the chest, which threatens to suffocate him. There is a short, dry cough, some wheezing, and distention of the lower zone of the chest. He sits up in bed or rises from it, and sits or stands, desires fresh air, and may open the window to obtain it. He draws it in with all the power of his inspiratory muscles.

When the attack is fully developed he sits with his elbows resting on his knees, his shoulders raised and fixed, his head forward on his hands or at times thrown back on the pillow. Or he may seek a chair, resting his elbows

on his arms and his head against the back. Whatever be the favorite position, it is usually maintained until the paroxysm subsides. The object of the position is to raise the shoulders and fix the scapulæ, clavicles, and spine, so as to enable the accessory muscles of inspiration to raise the ribs to the farthest possible extent and increase the capacity of the chest to the utmost. The face is pale and anxious at first, but soon becomes livid and swollen, with protrusion of the eyeballs, and as the attack continues the cyanosis becomes very great. There is a copious flow of nasal secretion that provokes sneezing. Profuse clammy perspiration breaks out and the extremities become cold. All these signs show the great strain to which the right heart is subjected.

The respirations become labored and the expiratory part prolonged; they are attended by a wheezing stridor, with sibilant and sonorous rales which may be heard outside the room. The chest is expanded, and on examination the lungs will be found extended downward, the heart and liver being also pushed down. The diaphragm is low and its movements are slight, especially in view of the strenuous inspiratory efforts made by the patient. Notwithstanding the dyspnœa, the respirations may be reduced in frequency, in some cases not exceeding half the normal number. This is owing to the greatly increased length of the expiratory part, which may be two or three or even four times as long as that of inspiration. The pause which normally follows expiration is absent, inspiration following immediately, but there may be a post-inspiratory pause.

The most striking signs to be noted on inspection are the great distention and very limited movement of the chest and the fulness and immobility of the abdomen, although the recti are in a state of strong tension. In inspiration, the soft parts, except the supraclavicular fossæ, are but little drawn in, and the epigastrium remains full; all in marked contrast to the recession of these parts observed in obstruction at the larynx or in the large bronchi. Percussion in all parts of the chest gives the hyperresonant note of marked emphysema, the area of cardiac dulness being reduced and hepatic dulness greatly depressed.

On *auscultation* instead of normal vesicular breathing, numerous dry, wheezing, piping rales are heard, most distinctly during expiration, and in some cases in the last part of inspiration. Rhonchus and sibilus develop later, soon followed by moist crepitation. These signs vary from time to time, shifting from place to place, owing to alteration in the spasm of the tubes, the degree of tumefaction of their lining membrane, or to temporary obstruction of bronchi by secretion.

The *voice* is weak and gasping on account of the difficulty of breathing, on which the patient is so intent that he can scarcely utter a word or move.

The attack lasts about two hours, often more, but rarely less. Gradually the intensity of the paroxysm abates and the distress grows less agonizing. Up to this time the patient is unable to cough; now the cough becomes possible and he expectorates small quantities of grayish mucus mixed with froth, in the midst of which are seen small, opalescent, gelatinous masses—the mucous perles of Laennec. The occurrence of expectoration indicates the termination of the paroxysm. Gradually the respiration becomes fuller and easier. The mucus is extremely tenacious at first, but gradually becomes more abundant and frothy until at length the paroxysm terminates. Usually there is a copious flow of urine with an abundant deposit of urates as the attack ends.

The patient now falls into a quiet sleep, to awake in the morning refreshed, although somewhat wearied.

Paroxysms may recur regularly at the same hour, continuing for several days or even weeks, at first mild, but growing more severe until they reach the height of severity, after which they gradually abate until they cease altogether. A paroxysm may end, as it began, suddenly, but more often it terminates gradually, especially the paroxysm of longer duration, owing to the greater amount of bronchial secretion caused by the bronchitis that has developed during the attacks.

The recurrences of the attacks of asthma are extremely variable. Few asthmatics escape them, but if the liability is growing less the intervals between the attacks lengthen until they cease altogether. Usually, however, the intervals grow shorter and in many cases the attacks grow in severity, but they may, on the contrary, become less severe. In many persons the attacks, at least in the early stage, occur at certain seasons of the year only, as with the approach of summer, and after a few years in the autumn as well. As the years pass they begin to recur at irregular and more frequent intervals. Fagge refers to a case in which the paroxysms recurred night after night for the last twenty-five or thirty years of the patient's life.

Sometimes the paroxysm continues several days with little abatement, causing much prostration. It scarcely ever terminates fatally. Fagge met with one case in which breathing ceased and restoration was only affected by artificial respiration. In cases with frequently recurring or protracted attacks, chronic affections of the respiratory organs develop, especially emphysema. The breathing is persistently somewhat labored, but typical attacks become increasingly rare, finally ceasing, leaving the patient emphysematous, with exacerbations of dyspnœa simulating the characteristic course of the asthmatic paroxysm. In time the heart becomes permanently dilated and the condition is the same as that of advanced emphysema.

In some cases the act of inspiration is more labored than expiration, or they may be equally laborious. In other cases there is little if any spasm of the inspiratory muscles, and yet the breathing is labored and accompanied by hissing rales in all parts of the chest, probably due to spasm of the bronchial tubes.

The *sputum* in a true asthmatic attack is quite characteristic. It consists of pellets of grayish-white, semitransparent, tenacious material like boiled tapioca, with a little fine, foamy, thin mucus. The pellets or perles are composed of dense mucus, usually arranged in a twisted manner, the Curschmann spirals, and contain the Charcot-Leyden crystals, degenerated epithelial cells, and leukocytes, of which the majority are eosinophiles. The spirals consist usually of a central solid thread, which may, however, show some vacuoles and around it the mucus is arranged as a spiral. The spirals vary in the completeness of their formation; some have no central thread or only an indistinct one, or the mucus around them may be arranged in an irregular and imperfect manner, but many show all the parts completely and beautifully arranged. The whole is composed of mucus, the central thread being first formed and therefore the most firm. The twisting has been attributed to a rotatory motion of the cilia of the small bronchi, the motion being made more effective in forming the spirals by the spasm of the bronchial muscles. Hoffmann would explain their formation by the assumption that the whole bronchial tree ends in spirals. If this were the case, minute examination of

the lungs should reveal such an arrangement. Curschmann regarded these spirals as occurring in asthma only, and as due to a special kind of catarrh of the finer bronchi. Hoffmann agrees with him and designates it "asthma catarrh." He quotes Schmidt's "investigation of a favorable case which showed that the epithelium of the smaller bronchi was well preserved and that the lumen was filled with a mass of mucus. The winding of this mass could be very nicely followed; it was found to be smallest in the finest bronchioles, and became thicker and thicker as the larger bronchi were approached. In the medium-sized bronchi, where cartilage plates begin to be found, there were seen in a cross-section several such winding figures formed by the union of several smaller bronchi. As typical central threads are found in small bronchi where there are no glands, the threads cannot be regarded as a secretion of the bronchial glands." All are not agreed that these spirals occur in asthma only; some observers report finding them in pneumonia and bronchitis, but the reports require confirmation. If they do occur in these affections it is evidently only in small numbers and not in the large numbers met with in asthma. They are found during the early stage of the asthmatic attack, disappearing when the sputum becomes more abundant and muco-purulent.

The *crystals* are colorless octahedra, small but varying in size, and denser than the other constituents of the sputum. They occur in groups which may be massed into a variety of shapes and appear as yellowish or yellowish-green spots. Their chemical constitution is uncertain, but as they occur in the spiral plugs with the degenerated cells they probably result from chemical changes in the latter. By keeping the sputum expectorated during an asthmatic attack in a moist chamber, crystals have occasionally been found to form where there were none previously. They occur almost always in association with the eosinophiles and both disappear together. They have been regarded as identical with spermin crystals, but the latter are larger and are rarely found associated with eosinophilic cells. Similar crystals are met with in leukæmic blood, and some observers report having found them in the sputum of bronchitis. Oxalate of lime crystals have also been found; their occurrence is not constant and is probably accidental.

The expired air contains no oxygen or at most only a trace, carbonic acid replacing it.

The catarrhal secretion may be very abundant from the beginning of the attack, constituting the *asthma humidum* of older writers; it may persist after the attack subsides. The patient may have periodical attacks of profuse expectoration without dyspnœa, lasting some hours. Slight *hæmoptysis* in the form of streaks of blood is not rare in severe paroxysms. The blood comes from the larger bronchi.

Trousseau first pointed out that asthma may begin as recurrent attacks of coryza with sneezing of extreme violence. The nose runs profusely; the eyes swell and fill with tears; then after a few hours the symptoms subside as rapidly as they set in. During the night a paroxysm of asthma comes on with the usual characters. This series of phenomena may repeat themselves for several days in succession. In some cases the coryza and lacrimation may constitute the whole paroxysm, at least for some time, after which the fully developed attacks of asthma occur.

Of the varieties of symptomatic asthma the most important is *hay asthma* or *hay fever*. It is often associated with typical bronchial asthma or may

alternate with it. Many cases beginning as hay asthma gradually change into the ordinary form of asthma, which may in time replace it altogether.

**Diagnosis.**—In the typical cases of asthma the signs and symptoms are so characteristic that the diagnosis is easily made. The paroxysmal nature of the attack, its sudden onset, the uncertainty of its occurrence, the expiratory dyspnœa with extreme prolongation of the expiration, the expanded and fixed chest, and the depressed, immobile diaphragm are pathognomonic. The presence of large numbers of eosinophiles in the sputum favors the diagnosis of asthma. Spirals and crystals are at least uncommon in other diseases. In *laryngeal* and *tracheal obstruction* the dyspnœa is inspiratory. The marked respiratory movements of the larynx in the laryngeal affection, the stridor of the inspiration instead of the wheezing of asthma, the contraction of the chest and elevation of the diaphragm instead of the extremely distended chest and the depressed diaphragm of asthma, serve to differentiate these conditions from the latter disease.

The diagnosis of *acute bronchitis* from asthma may present some difficulty, especially in children, in whom asthma is often atypical. The one often complicates the other, but in bronchitis the dyspnœa is not of sudden onset; it begins and ends gradually following the onset of the catarrh, and not preceding it. Diagnosis is important, as the depressing treatment of asthma may aggravate and prolong the bronchitis.

Asthma and *emphysema* so often co-exist that it may be difficult to estimate their relative importance in a given case. During the dyspnœic attack the sputum will serve to differentiate them; in the interval the respiratory capacity of the chest will be much reduced in emphysema and normal in uncomplicated asthma.

*Paroxysmal cardiac dyspnœa* is distinguished by the quick, panting respiration and the absence of prolongation of the expiratory act.

*Enlarged bronchial glands* in children may give rise to dyspnœa. In these cases there is usually a short, dry cough, dulness in the interscapular region; with irregular fever, wasting, and night-sweats.

*Mediastinal tumors* and *aneurism* of the arch of the aorta may, by compressing the trachea or left bronchus, give rise to paroxysmal dyspnœa of an asthmatic type, but it is usually irregular in its symptoms. The brassy cough characteristic of tracheal pressure is usually present, tracheal tugging is sometimes obtained, while dulness over the upper part of the sternum and a heaving impulse may be found.

A *foreign body* in a bronchus can usually be differentiated by the history. In such a case the signs are usually found only in one lung unless the inhalation of the foreign body has been followed by general bronchitis.

A *restless, disturbed sleep* may be a mild, although unrecognized, asthma. *Hysterical dyspnœa* with spasm of the diaphragm may lead to error if a hasty diagnosis is made. Both inspiratory and expiratory movements are short and there is inspiratory retraction as in laryngeal obstruction. There is no real dyspnœa. The onset of *influenza* may present a remarkable resemblance to asthma. The presence of spirals and crystals with eosinophiles in the sputum of asthma, and of Pfeiffer's bacillus in that of influenza, will determine the diagnosis.

**Prognosis.**—A paroxysm is rarely fatal. Hilton Fagge's remarkable case, in which artificial respiration was necessary to resuscitate the patient, has already been noted.

*Age* is of more importance in the prognosis than all other considerations, even the severity and frequency of the paroxysms, because elasticity of the lung and integrity of the myocardium are essential to prolonged resistance. The outlook is, therefore, less favorable after middle life. Asthma appearing in childhood may disappear at puberty, especially if the paroxysms are decreasing in severity, if the intervals between the attacks are long and increasing in length, and if the child leads a healthful life in a suitable climate.

In other cases the outlook depends chiefly on the degree of emphysema present and on the condition of the right heart. Not a few chronic asthmatic patients live to old age and die of some other affection. Much depends on the patient's environment. Under the most favorable circumstances many are completely free from paroxysms as well as of all symptoms of bronchial irritation, while in less favorable surroundings they may suffer more or less severely.

**Treatment.**—Asthma, like other nervous affections, requires variable treatment. Inexplicable idiosyncrasies are as frequent in the action of the remedies as in the action of the causes. One is reminded of the story told of Graves, who is said to have visited two asthmatic patients in the same day; the first attributed his attack to a smoking chimney and the other made his chimney smoke to relieve his attack.

The utter capriciousness of asthma in its response to the action of drugs renders our course of treatment largely empirical, so that in many cases, in the hope of finding one that will succeed at last, one drug after another is tried only to be discarded as useless. While this indicates the method that is generally pursued, the most successful course will be found to be to study each patient carefully in the hope of finding a clue not only to the cause, but also to rational and therefore more probably successful treatment.

The treatment should be directed as far as possible toward the removal of the exciting cause; if successful, complete relief from the affection is usually the result. Search should also be made for the so-called predisposing cause, or for the irritable point on which the exciting cause acts. This is found most frequently in the nasal passages, but may occur in many other parts, as the larynx, trachea, bronchi, stomach, etc. Wherever it is situated it should receive appropriate treatment so as to remove its pathological irritability. The patient's general condition may be at fault and should be restored as far as possible to normal.

In some cases much may be accomplished by systematic respiratory gymnastics in order to develop the capacity of the chest and probably improve the tone of the respiratory centre so as to render its equilibrium less easily disturbed. The judicious and regular use of cold baths to stimulate general vigor may prove of much benefit.

1. **Treatment of the Paroxysm.**—The distress is so great that it usually requires as prompt relief as possible. Patients instinctively turn to those agencies which their experience has taught them to be most effective.

The *hypodermic injection of morphine* usually gives the most prompt and permanent relief. An initial dose of gr. $\frac{1}{6}$ (0.01 gm.) generally suffices; it may be repeated in about two hours if necessary or a larger dose may be given if due relief is not experienced. A degree of tolerance soon occurs in some cases, but even in these rarely more than gr. $\frac{1}{4}$ (0.035 gm.) will be required. Its use rarely if ever leads to the morphine habit, yet the possibility of such an untoward result should be borne in mind. The existence of bronchitis

with much secretion in association with the asthma may render the use of morphine dangerous. In very severe paroxysms strychnine in large doses hypodermically, gr. $\frac{1}{20}$ to $\frac{1}{15}$ (0.0033 to 0.0043 gm.), with some morphine, may give most benefit.

*Atropine* subcutaneously, judging from the experiments of Brodie and Dixon, should be an effective remedy in allaying the bronchial spasm. It will require to be given in doses sufficiently large to cause full physiological effect. It might be combined with the morphine.

*Heroine* has of late years been much used instead of morphine and in many cases with gratifying results. It is an efficient respiratory sedative in bronchial affections, relieving cough and causing sleep. It may be given subcutaneously, gr. $\frac{1}{30}$ to $\frac{1}{6}$ (0.0033 to 0.01 gm.), and repeated in an hour if the paroxysm is not relieved. It requires the same precaution in its use as morphine.

*Chloral hydrate* has been found by some as efficacious as morphine in suitable cases. It is best given frequently and in small doses, gr. 10 (0.66 gm.) every hour for the first few doses, after that gr. 5 (0.33 gm.) until the paroxysm is relieved. It has a depressing effect on the respiratory centres, but unfortunately also on the heart, and therefore it should be given with care in cases with weak heart, if given at all.

*Cocaine* has been used as a local anæsthetic to the nasal passages and throat, but the *cocaine habit* is so easily acquired that its use is too dangerous to be recommended. The local application of an *adrenal* preparation, by causing constriction of the vessels, should prove of much value if the nasal mucous membrane is swollen and turgid.

A perle of *amyl nitrite*, or, probably better, of *amyl valerianate*, broken in a napkin or absorbent cotton and inhaled, or 3 to 5 drops of the fresh solution similarly administered, may bring at least temporary relief. Inhalation of a few drops of *chloroform* sometimes brings prompt and even lasting relief, but there is much danger of its use degenerating into a habit. Inhalations of *ether*, *turpentine*, *ammonia*, and *oxygen* have been used successfully. The efficacy of many liniments applied to the chest is doubtless due to their vapors being inhaled.

Sedative and antispasmodic remedies are largely used, the best being *stramonium*, *belladonna*, *lobelia*, and *tobacco*. Internally the tinctures of the first three require to be given freely, ♏ 10 to 15 (0.6 to 1 cc.), and even then they too often fail, especially in the sudden, infrequent attacks.

The fumes from these and many other similar remedies have long been used for the relief of the paroxysm. Various powders, cigarettes, and medicated papers are sold for the purpose. Stramonium, belladonna, and nitrates enter into the composition of most of them. Such efficacy as they possess depends largely on the nitrates and the active principles of the *solanaceæ* in the fumes. Trousseau found a few puffs of a cigar relieved his own attacks. Cigarettes of stramonium and camphor enjoy a reputation. A frequently used powder consists of a combination similar to the following: Stramonium leaves, ʒij (8 gm.); anise, ʒj (4 gm.); tobacco leaves, gr. iij (0.2 gm.); potassium nitrate, ʒj (4 gm.). A teaspoonful to be ignited in an open vessel and the fumes inhaled. The fumes of nitre paper, an old remedy, made by saturating blotting paper with a solution of potassium nitrate (1 in 15), give relief to some patients. Sée strongly recommended pyridin, 1 dram (4 cc.) being placed in a saucer in the middle of the room.

It is a disagreeable, nauseating remedy, liable to cause much depression, and is not therefore to be advised.

None of these inhalations is to be recommended, as at best they rarely bring more than temporary relief, and they may do injury by depressing the heart, whose labors are already fully taxing its powers. The vapor of warm water may prove much better than any kind of smoke. To it may be added such remedies as menthol, benzoin, and eucalyptol. The use of a hot hand-and-foot bath often brings considerable relief in a short time.

2. **Treatment in the Intervals of the Paroxysms.**—A careful search should be made for the exciting cause so as to remove or avoid it. The condition of the nasal passages demands first attention, as in not a few cases the seat of reflex irritation is found here, and the removal of abnormal conditions may be followed by cessation of the asthma. Too much must not, however, be expected from nasal treatment, and it should be undertaken only for the relief of demonstrable disease. Much injury may be, and has been done by the galvanocautery. Many patients experience temporary relief from the treatment and often are reported as cures, so that the literature has become unreliable.

The *diet* should be carefully inquired into; if any articles are found to induce an attack they should be excluded. Constipation should be relieved and the general health made as vigorous as possible, so that the stability of the nerve centres may be raised to the highest degree attainable.

The bronchial mucous membrane should be relieved of all traces of catarrhal inflammation. Cod-liver oil during the winter months may prove useful.

Schäffer is a strong advocate of the *faradic current*, an electrode being placed on each side of the neck about one inch below the angle of the jaw. The current should be fairly strong and used twice daily for fifteen or thirty minutes.

Any *locality* found to induce an attack must be avoided at all hazards. A dry, sandy soil, especially in a dry, pine district is usually most suitable for asthmatics. The district and climate most suitable for the individual must, however, usually be determined by his own experience. Many do well in the dry, bracing atmosphere of the western plains of Canada; others in the milder climates of Florida, Cuba, and California.

Of the drugs which have been used to prevent the recurrences of attacks of asthma, *iodide of potassium* has been of most service. It may be given in doses of gr. 5 (0.3 gm.) three times a day and gradually increased to three or four times that quantity. It often brings great relief, but it is doubtful if it alone ever effects a cure. Its use should be continued over long periods, two or more years, with a day's omission every eight or ten days. If there is freedom from paroxysms for a long time the dose may be gradually reduced. *Arsenic*, although much less esteemed, is the next most useful drug. In properly selected cases nux vomica in ascending doses is considered by Musser quite as valuable a remedy. The cardio-vascular remedies, such as digitalis, caffeine, and convallaria, are useful in cases of pseudocardiac asthma and also in true asthma when the circulation shows signs of failure.

The mental state demands close attention, as attacks are not rarely precipitated by causes acting on a weak will-power. Psychical treatment becomes of importance in these cases. This can only be carried out satisfactorily in a well-equipped institution where the aid of hydrotherapy, electrotherapy, etc., is available.

# CHAPTER XIX.

## DISEASES OF THE LUNGS.

By HOBART AMORY HARE, M.D.

### CIRCULATORY DISTURBANCES OF THE LUNGS.

**Congestion of the Lungs.—Etiology.**—As commonly employed, two quite different circulatory disturbances of the lung are included under the term congestion, which is therefore subdivided into the active and the passive types.

1. *Active Congestion* (Hyperæmia of some writers).—In this condition an increased amount of arterial blood is thrown into the lung and consequently it is found in the initial stage of all inflammatory diseases of the lung and pleura, as pneumonia, bronchitis, tuberculosis, and pleurisy. During the cold stage of the paroxysms in malaria and in other diseases accompanied by rigors an excess of blood is distributed to the lungs. The inhalation of excessively hot or cold air or irritating gases brings about the same state, at times very rapidly fatal. Violent exertion excites active congestion and athletes have died apparently from this cause alone. Affections of the pons or medulla are possible excitants of the condition and it may precede the fatal termination of coronary artery disease. A zone of hyperæmic tissue surrounds essentially every circumscribed lesion of the lung, whether pneumonia, tuberculosis, abscess, gangrene, or new-growth. That active congestion is ever a primary lesion, instead of a symptomatic affection, is extremely doubtful, although many French writers vigorously support this view. In cases of pure active congestion the morbid anatomy and histology of the affected part of the lung are essentially those found in the initial stage of croupous pneumonia.

2. *Passive Congestion.*—This is practically always due to faulty action of the heart, which may depend upon a weak right ventricle or upon obstructive or regurgitant lesions in the left side. To these as causes may be added non-aëration of the lung and compression of the pulmonary veins. Two important types of the condition are observed, (*a*) brown induration and (*b*) hypostatic congestion.

(*a*) Brown induration, also called mechanical congestion, accompanies lesions of the left heart which prevent the proper outflow of blood from the lungs. Histologically, the vessels of the lung are distended. The pulmonary connective and elastic tissues increase in amount. In the slowed blood of the distended veins, actual stasis appearing in some areas, increased hæmolysis occurs and pigment from the disintegrated red cells is deposited in the interstitial tissue and in the alveolar epithelium. Chronic bronchitis also ensues. The increased pulmonary and bronchial tissue causes induration; the pigment gives to the organ a brown color. When incised surfaces

of the lung are exposed to the air they become bright red from oxidation of the excessive amount of hæmoglobin. The sputum contains leukocytes and pigment-bearing cells which have become detached from the alveolar walls. From the nature of the affection primarily responsible for their appearance, the latter are by some writers called "heart-disease" cells.

(*b*) Hypostatic congestion is that form determined by gravity in addition to slowed pulmonary circulation dependent upon weak cardiac action and deficient aëration. It is not uncommon in prolonged febrile diseases, as typhoid fever, and in adynamic states in general. For the latter reason the aged are particularly prone to the affection. Prolonged recumbent posture for any cause, as in the treatment of fracture, favors this form of congestion. It has followed morphine poisoning and is particularly apt to occur in persons suffering from brain lesions, notably those which induce paralysis or coma. The posterior portions of the lungs, or the outer portion of one lung if the patient has laid on that side, are dark in color, heavy, pit on pressure, and on incision drip blood or bloody serum. The vessels are distended and the perivascular tissues contain an excess of serum. Under these conditions the serum and less often some blood passes into the vesicles, the air is thereby expelled, and the part sinks when placed in water. To this condition the terms hypostatic pneumonia and splenization have been applied, the latter possibly being appropriate only when considerable blood is in the vesicles. The alveolar epithelium shows granular degeneration and usually more or less extensive desquamation.

**Symptoms.**—Active congestion of the lungs is characterized by sudden onset, beginning as a rule with a chill and rapidly developing dyspnœa, which is accompanied by sharp pains in the side, cough, and expectoration. The sputum is frothy and contains blood. The temperature may rise to 103° or even higher, but the fever does not persist, falling by crisis on the third or fourth day. Aëration of the lung is diminished, so that cyanosis together with distention of the superficial veins of the neck may be well marked.

The thorax may be somewhat distended, and upon percussion some impairment of resonance may be heard. Upon auscultation the breath sounds will be found to be harsh and rough, and rales of various kinds may be detected; thus at the base of the lungs fine crepitant or subcrepitant rales may be distinctly audible, while over other parts sibilant and sonorous rales may be detected. Vocal fremitus may also be somewhat impaired. In some cases of active hyperæmia the pleura is considerably involved, so that friction fremitus is heard. A slight exudate may also take place. To this form of the affection the late Dr. Potain, of Paris, gave the name of pleuropulmonary congestion.

It is evident, therefore, that primary active congestion developing after exposure to cold or injury is, at the beginning of its evolution, not unlike genuine pneumonia.

The symptoms of passive congestion consist in slight shortness of breath upon exertion, and a hard, usually dry cough, which has a tendency to become exacerbated upon the slightest provocation. Expectoration varies; at times it may be slight or absent, and again it may be of moderate degree. In the latter instance the sputum frequently contains blood. Attacks of hæmoptysis may also occur. The vesicular murmur may be diminished and moist rales be plainly heard over the base of the lungs. If the cardiac

lesion is aortic instead of mitral, symptoms of pulmonary œdema many manifest themselves.

The symptoms of hypostatic congestion are not definite. As hypostasis develops very slowly in many cases, nothing but slight acceleration of respiration may be present for some time; but when its evolution is more rapid, as for instance in the acute infectious diseases, a pronounced degree of dyspnœa together with cyanosis may appear with comparative suddenness. As soon as exudation occurs and the fluid gravitates, increased fremitus, dulness, and the presence of moist and crepitant rales will be found. The vesicular murmur also is diminished or perhaps absent.

**Diagnosis.**—In regard to active congestion, it is evident from what has already been said that the affection possesses no distinctive characteristics. In the beginning it may resemble pulmonary infarction or genuine pneumonia, but as it progresses it will be readily distinguished from both these diseases. From infarction it is differentiated by the disappearance of bloody expectoration and subsidence of other symptoms within a much shorter period than is the case in the former disease. Absence of hepatization and the occurrence of crisis on the fourth or fifth day will serve to distinguish it from croupous pneumonia. The initial chill is said to be less violent than in pneumonia. Primary congestion of the lungs differs from bronchopneumonia both in the manner of onset and evolution, and these differences constitute a means for differential diagnosis. The diagnosis of passive congestion will be made easy by the discovery of the causative cardiac lesion.

Difficulty of breathing and cyanosis developing during the course of an adynamic disease should always arouse suspicion of hypostatic congestion, particularly if no elevation of temperature occurs in association with the other symptoms. From pleural effusion developing in the course of such an affection or in bronchopneumonia, hypostatic congestion can be differentiated by the fact that the level of dulness changes when the patient changes his posture; in effusion too the percussion note is duller than it is in hypostatic congestion.

**Prognosis.**—In active hyperæmia the prognosis is usually favorable, but in some cases œdema may develop with fatal result, or pneumonia be superimposed upon the congestive process, thereby rendering the prognosis less favorable. A few cases following a sudden chill which resulted from exposure to cold when the patient was in an overheated condition have been reported as terminating fatally within a few hours. As a rule, however, the symptoms subside within a few days and complete recovery results. Nevertheless, the affection is always to be looked upon as serious, and one demanding active treatment. The prognosis of passive congestion depends largely upon the condition of the heart, which is responsible for it. Owing to the lessened resistance of the pulmonary tissues, pneumonia may develop and cause speedy termination of life.

In hypostatic congestion the prognosis varies with the condition in which it develops, with the vitality of the patient, and the promptness with which the pulmonary involvement is discovered and treated. In the case of old and feeble persons the disease is almost invariably fatal, and in young children the mortality is also very high.

**Treatment.**—In active congestion prompt measures must be taken to arrest the hyperæmic process. For this purpose cups should be applied

over the entire pulmonary area. If marked cyanosis is present venesection may be resorted to with good results. If the initial intensity of the symptoms yields, then a stimulating expectorant, such as ammonium chloride, may be employed with advantage, or if preferred the carbonate of ammonium may be used instead of the chloride. Concentrated liquid nourishment must be provided. The dietary mentioned in the article on bronchopneumonia is appropriate.

In regard to the treatment of passive congestion measures directed to the causative cardiac affection are the ones which will most favorably influence the pulmonary condition. Moderate doses of digitalis together with small doses of strychnine will do good service. Ammonium chloride or benzoate with a small dose of codeine or heroine may be useful in allaying the chronic cough. Intercurrent attacks of acute bronchitis are to be treated in the usual manner.

As concerns hypostatic congestion, it may be stated that prophylaxis is quite as important as treatment. Aged or feeble persons who are confined to bed should not be allowed to lie long in one position, but should be made to assume a different posture every hour or two. The slightest manifestation of bronchitis in such persons should immediately lead to the institution of treatment. When the disease has once developed the primary indication is to support the heart, and for this purpose digitalis should be given. Hoffman's anodyne is also of value. It may be given every hour in dram doses and digitalis given every four hours, ♏ 10 (0.6 cc.) of the tincture being administered until its effect becomes apparent and the frequency of its administration being reduced in accordance with the indications of the individual case. Dry cups should be applied over the base of the lungs posteriorly. Active purgation may do good if the patient's strength is not too low to permit it. In nearly all cases a brisk mercurial purge will do no harm and may do good. If the patient is strong enough, hydragogue cathartics such as magnesium sulphate may be used.

**Œdema of the Lungs.—Etiology.**—Localized, collateral, or focal œdema occurs in the tissue surrounding circumscribed lesions of the lung, as inflammatory areas, new-growths, abscesses, infarcts, and tuberculosis, being congestive and in some instances toxic or inflammatory in origin. General œdema, either acute or chronic, is not so readily explained. In the chronic form it accompanies chronic pulmonary congestion, chronic nephritis, cachexia, anæmia, cerebral disease, and chronic infections. In cases of slowly oncoming death it occurs as the so-called terminal œdema. Regarding this type, Coplin's statistics indicate that too large a percentage of cases has been attributed to this relatively unimportant cause, with the result that an undeservedly lessened significance has become attached to pulmonary œdema as a whole. In 2030 autopsies, most of them upon persons dead of chronic diseases, œdema was found in but 405, or 20 per cent., leaving 80 per cent. of deaths unaccompanied by noticeable accumulation of serum in the lungs. Disease of the heart is the most frequently preceding lesion, that organ being affected in 350 of Coplin's 405 cases.

Acute pulmonary œdema occurs particularly in connection with diseases of the kidneys or arteries, although other predisposing causes are alcoholism, extreme cold, and intense mental emotion. Hysteria has been cited as a cause. Of practical interest is the œdema following anæsthesia, particularly that induced by ether, and the form developing with various infectious

diseases, as typhoid fever, pneumonia, bronchitis, scarlet fever, and influenza, this being in favor of the belief that the condition is toxic in origin. This view has been ably upheld by French writers, while most German observers prefer the mechanical theory as an explanation. The classic experiments of Welch led him to believe that pulmonary œdema is due to increased capillary tension produced by an excess of blood from the right heart over that handled by the partially disabled left ventricle. This is a plausible explanation in some cases, especially the terminal œdemas. Recent studies point to the action of toxins as being an additional if not a paramount factor in many cases of the affection. Welch himself now speaks of the frequency with which bacteria, apparently in colonizing numbers, are found in œdematous lungs. The acute pulmonary œdema produced experimentally by the injection of adrenalin very closely simulates that in human beings, but in its development we must admit that mechanical and toxic effects are possibly combined, and hence this cannot be regarded as a type of the condition due purely to circulatory disturbance. On the whole, the most acceptable view as to the etiology of pulmonary œdema is that it is due to increased capillary tension accompanied, aided, and probably in many instances preceded, by degenerative changes, toxic in character, of the capillary endothelium.

**Morbid Anatomy.**—The base of the lung posteriorly is chiefly affected, but the entire organ may be involved. The œdematous lung is heavy, boggy to the touch, and pale in color unless darkened by associated congestion, which is frequently present. It pits on pressure and is readily incised. From the incision an abundance of frothy serum flows. At first this is almost clear, but later, especially if pressure upon the lung be made, it becomes blood-stained; the degree of congestion determines the prominence of this feature. The bronchi contain frothy fluid which may be blood-stained. Crepitation is always lessened, but is often present throughout the organ; small patches may be airless. These if excised will sink in water, but they are commonly so small that care in excision is necessary to prevent expressing the fluid. Occasionally the affected areas are gelatinoid in consistency, due to partial and probably postmortem coagulation of the œdema fluid; in them, however, fibrin is never abundant.

Microscopically the bloodvessels may be distended, although usually this is not conspicuous and often is entirely absent. The fibrils of the connective tissue are widely separated by the distended lymph spaces. In the alveoli are few or many leukocytes, variable in type, and a small quantity of residual granular material from the serum. Fibrin may be present, but never in large quantities. The alveolar epithelial cells may be granular and always show more or less extensive desquamation. Red blood cells are usually scanty except in cases of acute fulminating œdema, when they are commonly numerous. This accounts for the conspicuous reddish color of the frothy fluid which is often expectorated in extraordinary quantities in these cases. Slight catarrhal bronchitis may be manifest. In the bronchial walls and peribronchial structures, including the lymph nodes, the presence of an excessive amount of serum is evident.

**Symptoms.**—The symptoms of acute œdema consist in rapidly developing dyspnœa, cough, and expectoration. Breathing is very difficult and becomes progressively worse as the exudate continues to accumulate. The patient is anxious and terrified and is fully conscious of the danger which

threatens him. As the œdema increases the pulse becomes weak and small, cyanosis changes to lividity, a cold sweat breaks out over the body, the extremities become icy, consciousness is lost owing to carbonic-acid poisoning, and death ensues under all the manifestations of profound asthenia. The temperature is usually subnormal.

In cases of very rapid evolution, a class to which French clinicians have applied the term hyperacute œdema, a fatal termination may occur within a few minutes after the onset of symptoms. The manifestations of œdema of the lung occurring as the terminal event of exhausting diseases are usually not so violent as those just described, the onset and evolution being more gradual, and the symptoms less pronounced. Expectoration is usually profuse, contains a high percentage of albumin; it is often of a pink or red color.

The physical signs are not characteristic. Upon percussion normal resonance is found to be diminished, particularly over the posterior portion of the lungs. Occasionally small patches of tympany may be found interspersed throughout the dull area. Upon auscultation various kinds of rales—fine and coarse, mucous, bubbling, and crepitant—will be heard.

**Diagnosis.**—An adequate history together with the symptoms and physical signs just mentioned will in the majority of cases suffice to make diagnosis clear.

Acute œdema might be mistaken for pulmonary embolism, which also has a sudden onset marked by severe dyspnœa. The difference in the character of the sputum and the not uncommon absence of physical signs, or the difference in their character when they are present, will serve to distinguish the latter affection. In uræmia the results of the urine examination and the presence of Cheyne-Stokes breathing will afford a means of differential diagnosis. Although the symptoms of hydrothorax are in some respects similar to those of œdema of the lung, the physical signs are different; dulness is more pronounced and its limits vary with the posture the patient assumes. The hyperacute cases, which are fatal in a few minutes, may be confounded with cardiac paralysis or angina pectoris, and postmortem examination be required to disclose the cause of death. Of course, if the physician is fortunate enough to see the patient while he is still alive the nature of the trouble may be determined.

**Prognosis.**—Prognosis depends upon the underlying causative affection. It is always grave, no matter upon what condition it may depend.

**Treatment.**—Treatment must be directed both to the immediate source of danger to life—that is, to the œdema, and to the causative affection. For the first purpose, counterirritation in the form of dry cups or a large mustard plaster should always be employed, and in the more urgent acute cases venesection may be used with advantage. When cups are used they should be applied over the entire posterior pulmonary area. Inhalations of oxygen may be tried in the hope that they will allay dyspnœa. The heart must be stimulated by camphor and ether administered hypodermically. A solution containing 1 grain of camphor to 10 minims of ether is well adapted for ordinary use; 10 minims of this solution may be injected beneath the skin every half-hour. Atropine is another drug of value in the treatment of this condition. It is the writer's practice to give gr. $\frac{1}{60}$ (0.0012 gm.) hypodermically for the first dose and then use a smaller quantity at the end of three hours if indications for its employment are still present.

If life is prolonged, strophanthus and strychnine together with hydra-

gogue cathartics, and diuretics, if renal disease be the underlying causative affection, may be used according to the indications of the individual case.

**Hæmoptysis.—Etiology.**—The term hæmoptysis should be limited strictly to the phenomenon of blood spitting, but is by common consent interpreted as meaning the ejection of blood in any quantity coming from the respiratory tract. The numerous causes include:

1. Pulmonary tuberculosis, which is by far the most frequent single cause of hemorrhage from the lungs. Usually, the blood comes from eroded vessels which either lie in the walls of cavities, but less advanced disease may cause the symptom. Occasionally, the walls of small vessels infiltrated by the tuberculous process, instead of becoming thrombosed, as they usually do, rupture and give rise to hemorrhage. From this source the quantity of blood is commonly sufficient only to color the sputum, but small quantities of almost pure blood may be expectorated. Stress is placed by some writers upon aneurismal dilatation of vessels in the tuberculous areas as predisposing to rupture and consequently to hemorrhage. While this change undoubtedly occurs in the vessels of some cavities, its great frequency is not predicated by autopsy findings.

2. Ulcerative lesions of the larynx, trachea, or bronchi. These usually lead to slight hemorrhage only, but in some cases a vessel of size sufficient to cause serious or fatal loss of blood is eroded. Fibrinous bronchitis may give rise to profuse hemorrhage when the cast is expectorated.

3. Chronic lesions of the heart, especially mitral stenosis, not infrequently give rise to hemoptysis which may occur at intervals for years. The quantity of blood is commonly small.

4. In the initial stage of various inflammatory lesions, as croupous pneumonia, the sputum is often blood tinged.

5. Abscess or gangrene of the lung.

6. Trauma in the shape of blows upon the chest, or falls, or wounds of the bronchi or lung by foreign bodies aspirated or penetrating from without; under the last grouping is to be included puncture by broken ribs.

7. Leprosy and actinomycosis are among the rarer causes.

8. Malignant growths of the lungs or of the air passages. Ulceration of the tumor may be the direct cause of hemorrhage in these cases, but intrapulmonary growths may produce it by virtue of the surrounding hyperæmia or congestion.

9. Emphysema is an unusual cause of pulmonary hemorrhage. When occurring, the amount of blood is commonly small, but the condition has proven fatal.

10. Recurring hæmoptysis in subjects of chronic arthritis has been observed.

11. Pulmonary hemorrhage has followed heavy lifting.

12. Bronchiectasis is occasionally complicated by hemorrhage.

13. Diseases accompanied by hemorrhages elsewhere, or by hemorrhagic tendencies, as scurvy, leukæmia, and purpura, may cause troublesome bleeding from the lungs.

14. Hemorrhagic infarct of the lung may give rise to hæmoptysis.

15. In cases of arrested menstruation, the lung may be the seat of vicarious hemorrhage without showing a definite lesion.

16. During pregnancy and occasionally in some other conditions, hæmoptysis without discoverable lesions is encountered.

17. Ware in particular has called attention to pulmonary hemorrhage occurring in young persons who are healthy so far as diagnostic methods are able to determine and who do not afterward suffer from tuberculosis. Of 386 persons exhibiting pulmonary hemorrhage, 62 recovered from that affection and did not later develop tuberculous lesions.

18. Hysteria in some instances appears responsible for pulmonary hemorrhage. The case recorded by Pende is unique. A rugged girl of seventeen developed recurring hæmoptysis subsequent to the death of a sister from pulmonary tuberculosis. Stigmata of hysteria were present and signs of pulmonary lesion were absent. The hæmoptysis was for a time controlled by suggestion, but finally proved fatal. Autopsy revealed no lesion of the lungs.

19. Aneurisms of pulmonary or neighboring vessels rupturing into the lungs. Among these may be mentioned the aorta, pulmonary artery, the innominate, carotid, and even the subclavian, and the bronchial arteries. From these sources the hemorrhage may be relatively slight if from a small vessel or the partially thrombosed contents of an aneurismal sac of a large artery, or it may be rapidly fatal if a large sac ruptures.

20. Pulmonary distomatosis. This condition, known from the cause and the symptoms as parasitic or endemic hæmoptysis, is due to the presence in the lung and bronchi of the *Paragonimus westermanii*, one of the flukes. Hæmoptysis occurs in most cases of the affection, which is met with mainly in Japan and China.

**Symptoms.**—The circumstances under which hæmoptysis occurs, as well as the physical signs associated with it vary with the cause upon which it depends. The bleeding may be very slight or profuse. Thus when it develops as an initial manifestation of phthisis it is often slight, in bronchiectasis it is usually of moderate degree, in advanced phthisis and rupture of an aneurism it is copious.

As a rule it is sudden in onset, the mouth all at once becoming filled with blood. Persons who have already had attacks, however, may experience prodromal symptoms which warn them of the impending hemorrhage. They have a sense of tightness and constriction in the chest, some difficulty of breathing and a general sense of lassitude. Soon a sensation of tickling or pricking in the throat ensues, the patient becomes conscious of a salty taste, and the mouth suddenly becomes filled with blood. During an attack the patient is excited and anxious. Unless he is bleeding profusely or unless the hemorrhage has continued for some time, the face is flushed and the pulse rapid. This quickening of the circulation is no doubt partly due to the mental perturbation which is usually present. When a large quantity of blood has been lost symptoms of asthenia are observed; the pulse is then weak, the face blanched, the extremities cold, and syncope may supervene.

Bronchial hemorrhage due either to ordinary severe bronchitis or to cardiac disease does not give rise to symptoms of any consequence unless the alarm which not uncommonly develops may be considered as such.

The physical signs, as already stated, vary with the cause. They have been described under the different maladies with which hæmoptysis is associated. Palpation and percussion ought not to be practised during an attack of pulmonary hemorrhage.

**Diagnosis.**—The most important matter to be determined is whether the blood comes from the lungs, and if so then to ascertain upon what cause the bleeding depends. The principal condition from which hæmoptysis

is to be differentiated is hæmatemesis. If the patient be seen during the attack it will be comparatively easy to distinguish between the two by the difference in the character of the blood. Small quantities of blood from the lungs are bright red in color, frothy, and of alkaline reaction. If the hemorrhage be copious the associated symptoms and the history of the case will make the nature of the trouble plain. It must be borne in mind that no reliance whatsoever is to be placed upon the accounts of the patient or his friends in regard to the character of the attack of hemorrhage and the quantity of blood lost. It is not rare to be assured that the patient "bled about a quart," whereas the nurse in attendance upon the patient could prove positively that only a few ounces were lost.

In regard to the cause of the bleeding, a careful history, together with a subsequent physical examination, will be of the utmost value. Thus if a first attack has been preceded by cough, night-sweats, and loss of flesh the presumption that tuberculosis is the underlying cause will not be improbable. In like manner the discovery of cardiac trouble may explain the origin of certain mild cases. In slight cases of blood spitting the nose and pharynx should always be examined, as the causative lesion may thus be found. Detection of spurious hæmoptysis will depend upon the physician's acumen and knowledge. Blood spitting occurring in a neurotic or hysterical woman is always suspicious and should put the physician on the alert.

**Prognosis.**—Prognosis depends entirely upon the underlying cause. Although patients are always apprehensive of death during an attack of pulmonary hemorrhage it is very rare for early attacks to terminate fatally. Out of 386 cases observed by the late Dr. Ware, of Boston, only 3 resulted in death during early attacks. Of course, death may take place at once if an aneurism ruptures or a large vessel becomes eroded. So, too, if blood accumulates in a large cavity respiration may be seriously impeded, pneumonia develop, and death result within a few days. In advanced tuberculosis long-continued profuse bleeding may so weaken the patient as to cause his death.

In marked contrast to these unfavorable effects of hæmoptysis are the results of moderate or slight hemorrhage in cardiac disease. Not only do they do no harm, but they frequently afford relief. The writer is also convinced that temporary relief is often experienced by patients affected with early tuberculosis.

**Treatment.**—This depends upon the causative factors. In all cases rest is of primary importance. Moreover, if the patient is bleeding and frightened much good will be accomplished if the physician will first of all allay his fears by assuring him that in all probability the attack is not dangerous. Mental excitement and bodily restlessness will thus be overcome and nature given a better chance to exert her curative influence. A hypodermic injection of gr. $\frac{1}{4}$ (0.016 gm.) of morphine should be given at once in cases of any severity. It not only quiets the patient, but also allays the cough and thereby prevents fresh attacks of bleeding. If the action of the heart is tumultuous an ice-bag may be applied to the præcordium and gr. $\frac{1}{100}$ (0.0006 gm.) of nitroglycerin given every three hours until the blood pressure is lowered and the circulation subdued. Pieces of ice may also be swallowed.

In hemorrhage due to congestion counterirritation in the form of dry cups will be found useful. Arterial sedatives, such as chloral, aconite, or veratrum viride, may also be employed with advantage in certain cases. Ergot and

astringents, such as lead acetate and gallic acid, are valueless and should not be used. It is doubtful whether chloride of calcium is of any use. Certainly no one would think of giving it to arrest bleeding from a vessel of any size in another part of the body.

When blood spitting is due to cardiac disease no treatment other than that directed to the heart is indicated; as already stated, this form of hemorrhage is usually beneficial.

**Embolism, Thrombosis, and Infarction of the Lung.—Etiology.**—Hemorrhagic infarction or infiltration of the lung (pulmonary apoplexy) is the result of embolism or thrombosis of a branch or branches of the pulmonary artery; the former condition is much more frequently the cause. Emboli may arise from any part of the venous system of the body, thrombosis being the usual primary lesion, the veins of the leg and the uterus and para-uterine tissues being the most common sites. Emboli also originate in the right heart, particularly in the auricle, and in the pulmonary artery. Numerous cases of fat embolism following surgical operations or fractures of bone are on record and fragments of tissue, especially the liver, have been found in pulmonary infarcts. Regarding the frequency of pulmonary apoplexy as compared with the general processes of thrombosis and embolism in the body, it is to be remembered that very small emboli lodging in the lung may give rise to no clinical evidence of infarction, and that massive emboli occluding large arteries cause death so quickly that infarction cannot occur. Thrombosis in the pulmonary arteries, depending on pathological changes in their walls, is rare. Aufrecht maintains that these changes are due primarily to weakness of the heart resulting from endocarditis, myocarditis, pericarditis, or atheroma of the aorta. Whether or not the sequence of changes is as depicted by him, certain it is that the occurrence of pulmonary infarct is favored by enfeebled circulation and that it is most common in chronic heart disease.

**Morbid Anatomy.**—In the case of embolism of the large arteries, with sudden death, the lung may show no noteworthy changes other than the presence of the occluded vessel. The right lung is most often the seat of infarct unless in one of various possible ways the blood current in the right pulmonary artery is weakened. Infarcts are commonly in the periphery of the lung, the posterior edge at or near the base being a frequent site, but they occur in the interior of the organ. They may be single or multiple and vary in size from 1 to 6 cm. in diameter, although rarely a large part of a lobe is involved. They appear beneath the pleura as approximately circular, elevated, dark-red or blackish masses that in consistency are quite solid. On section they are more or less perfectly wedge-shaped, the typical infarcted area forming a cone with the base toward the pleura. In some instances, owing to the abundant collateral circulation of the lung, the area is almost globular. At or near the apex of the infarct may often be found the plugged vessel responsible for the lesion. Occasionally, however, careful search fails to reveal such obstruction and in some cases a possible source of emboli is not apparent. These instances are cited in support of the opinion that laceration of bloodvessels may, in the absence of obstructive lesion, cause pulmonary apoplexy, but this view cannot be regarded as established. As a rule, localized pleurisy develops over the affected area and a zone of œdematous lung surrounds the infarct. This zone may be also hyperæmic, thus giving to the enclosing band a reddish color as contrasted with the dark

# PLATE III

Hemorrhagic Infarct of Lung.

hue of the central area. As the infarct ages, the color fades because of disappearance of the blood pigment in the extravasated red cells and small infarcts may return almost to the normal hue. Microscopically the alveolar septa and the vesicles are suffused with blood, the latter accounting for the hæmoptysis which so frequently accompanies the process. In cases of fat embolism oil may be detected in the sputa.

The termination of the simple infarct consists in the disintegration and removal of the red blood cells by phagocytosis or absorption, often with resulting pigmentation of the surrounding pulmonary tissue or neighboring lymph nodes. The embolus may undergo resolution, and if the infarct was small the part may become approximately normal; that the circulation is ever perfectly reëstablished is doubtful. Fibrous tissue formation in the area is nearly always more or less pronounced, in some cases resulting in the substitution of the normal tissue by an irregularly contracted scar. Cases in which the entire infarct separated from the surrounding healthy tissue have been reported. Abscess or gangrene results if pyogenic or putrefactive organisms respectively gain access to the area. If the embolus is composed of tumor cells, a secondary new-growth develops in addition to the changes common to non-infected infarcts.

**Symptoms.**—These vary with the size of the vessel occluded and with the nature of the embolus or thrombus. When the pulmonary artery or one of its large branches is suddenly clogged, the patient is seized with a sense of suffocation and intense dyspnœa and may die within a few minutes. In other cases an attack of syncope comes on; the patient suddenly experiences a feeling of faintness, utters a cry, falls to the ground, and never regains consciousness.

Sometimes when a smaller branch is occluded the onset and termination is not so violent. Symptoms of asphyxia varying in intensity with the size of the vessel which is obstructed are the cardinal manifestations, but the patient does not succumb at once, life being prolonged for several hours. A person affected with this form of embolism or thrombosis presents a striking picture. Respiration is intensely labored, the face is livid, the veins of the neck distended, the nostrils dilated, and the eyeballs protrude from the sockets. The action of the heart is weak and rapid; as the asphyxia advances a cold sweat may break out over the body, it being often the precursor of death. Convulsions have also been known to precede death.

In case small bloodvessels are obstructed infarction results. Very often the first symptom complained of is pain in the side; this is soon followed by difficulty of respiration and within a few hours, by the development of cough and expectoration. The sputum is always blood-stained and is very often entirely sanguinolent, the blood and mucus being intimately mixed. This form of expectoration usually continues for several weeks, but as the infarct undergoes resolution it diminishes in quantity and gradually loses its sanguinolent character. During the course of the affection it is not uncommon for attacks of hæmoptysis to occur, but as a rule the quantity of blood lost is not large. In many cases the temperature is not disturbed, but in others slight elevations may take place; they are usually not of long duration. Infective emboli or thrombi may of course produce suppuration or gangrene, in which case hectic fever may be present. Infection of an infarct may also take place through the air passages and likewise give rise to fever.

Pneumonia and pleurisy may develop as complications.

**Physical Signs.**—In the rapidly fatal cases the physical signs are *nil*. In those cases in which life is prolonged a few hours the breath sounds first become weak and then the signs of congestion and œdema develop, so that large bubbling rales and crepitation may be heard. A systolic murmur is also frequently present, being due no doubt to the impact of the blood current upon the obstruction in the pulmonary artery.

In case of infarction, dulness will be elicited over the diseased area of the lung. Upon auscultation it is found that the breath sounds are impaired, or perhaps the vesicular murmur may be entirely absent over a circumscribed area. If an area of considerable size be involved bronchial breathing may be heard. Subcrepitant and crepitant rales can frequently be detected.

**Diagnosis.**—The cases in which the pulmonary artery or one of its large branches is suddenly occluded must be recognized by the presence of the symptoms described as belonging to this class of cases. When the patient is known to have suffered with phlebitis or endocarditis no doubt need be entertained in regard to the cause of his sudden illness and death. Naturally death under similar circumstances may result from angina pectoris, cerebral anemia, or sudden acute pulmonary œdema, and the possibility of these affections must be borne in mind. The difference in the type of respiration will serve to differentiate the affection from laryngeal obstruction due to œdema of the glottis. The existence of pulmonary infarct will be made plain by the sudden attack of costal pain and dyspnœa, the expectoration of bloody sputum, and the physical signs which have just been enumerated.

**Prognosis.**—Large emboli usually cause death in the manner previously described, although occasionally obstruction of a vessel of considerable size may be followed by subsidence of symptoms within a few hours. In these cases the embolus or thrombus becomes disintegrated and is resorbed. The prognosis of pulmonary infarction cannot be considered unfavorable, unless it be due to septic emboli. As a rule resolution occurs, the symptoms subside, the physical signs disappear, and recovery takes place.

**Treatment.**—Great care should be taken to prevent the occurrence of embolism and thrombosis. Care should be taken to secure good contraction and involution of the uterus after delivery. In case phlebitis develops, absolute rest together with immobilization of the affected part should be secured and treatment in accordance with the recognized principles of surgery instituted. Those affected with endocarditis should be enjoined to avoid violent exertion of every kind. Absolute rest is of the utmost importance in treating cases which have actually developed, and for this reason when a patient is seen in an attack he should not be disturbed for the purpose of having a thorough physical examination made.

The principal indication is to support the heart, and for this purpose the diffusible stimulants are most appropriate. Camphor and ether may be given hypodermically, and large doses of aromatic spirit of ammonia may be administered internally. If the patient survive a few hours strychnine and caffeine may then be used. If much restlessness is present a dose of morphine may be given, provided that marked cyanosis is not present to contra-indicate its use. Counterirritation in the form of dry cups may be useful by dilating the peripheral vessels and thus causing an afflux of blood to the surface. If great tension of the right side of the heart is present venesection may afford relief.

For those who survive, rest, nourishing food, and the use of strychnine and caffeine, as already stated, are the appropriate therapeutic measures.

The treatment of infarction is entirely symptomatic. For the pain in the side a mustard plaster or dry cups will often prove beneficial. Sometimes morphine or heroine may have to be used to relieve it. If there is much hemorrhage moderate doses of turpentine, for instance twenty drops three times a day, may be used with advantage.

## BRONCHOPNEUMONIA.

**Etiology.**—Under the terms bronchopneumonia, lobular pneumonia, catarrhal pneumonia, and capillary bronchitis, is included an affection so varied in cause and, although to a lesser extent, in pathology as to lead to the suggestion that it be called a lesion rather than a disease. If from these titles, however, bronchopneumonia be chosen, and for many reasons it is the preferable term, the name itself is significant and limits the disease to a quite definite process, even although the causes are exceedingly diverse. Bronchopneumonia, then, is an affection of the lung in which the usual sequence of events is that an inflammation of the smaller bronchioles in scattered areas is succeeded by involvement of anatomically related or of contiguous vesicles. In cases of the primary form the lesion in the two situations possibly begins more nearly simultaneously, but even here the pathology indicates that the exudate first appears in the bronchioles. As to mode of origin the disease is of two types, the primary and the secondary.

Primary bronchopneumonia includes about one-third the cases. In Holt's series of 443 cases, 154 were of this type, agreeing with Conner's conclusion that 30 to 35 per cent. of reported instances are primary. This type comes on without previous general disease, affecting robust healthy children mainly under two or three years of age. The cause in many instances is the pneumococcus, in this, as in the mode of onset, the affection resembling croupous pneumonia.

Secondary bronchopneumonia is due to many different causes, chief among which are the acute infectious fevers of childhood, particularly measles, whooping-cough, diphtheria, and scarlet fever. The age incidence of these diseases determines that of this type of bronchopneumonia which is chiefly in children below five years of age, although it of course occurs later in life; the latter is especially true of that in typhoid fever, smallpox, and erysipelas, although these diseases are not nearly so frequently complicated by bronchopneumonia as are those of the first group. In addition to these cases of bronchopneumonia occurring in the course of infectious diseases is a second group caused by the entrance into the lung of foreign materials and known as aspiration or deglutition pneumonias. These occur in subjects of all ages. In the first fluids are drawn into the lung. They may be derived from the mouth in cases of infection of that cavity or during operations about the mouth or throat conducted under anæsthesia. In other instances the material comes from the lung itself in the shape of fluid from bronchiectatic cavities, blood from pulmonary hemorrhage, or even pus which finds its way into the larger passages. In the deglutition pneumonia solid particles of food gain entrance to the lung. Either fluid or solid material from tumors in the larynx or œsophagus may thus induce bronchopneu-

monia. Both the aspiration and deglutition forms of the disease are really due to bacteria which pass into the lung with the other material. Some writers prefer not to class these types with bronchopneumonia, but other than the fact that they occur less often than the primary and the other types of the secondary form and finally develop suppuration there appears no valid reason for their exclusion.

In addition to these fairly definite causes of bronchopneumonia there are a host of less positive, but nevertheless important, predisposing factors which may play a part in all cases and which in some are of great significance. Age is an important factor. As already stated, young children are particularly the subjects of the disease for the reason that the primary affections causing it by inducing bronchitis are so prevalent among children under five years of age. Whenever epidemics of measles, diphtheria, or whooping-cough occur there will be a corresponding prevalence of bronchopneumonia. The primary type of the disease is confined almost entirely to very young children. In a second class of age incidence are old persons, the extremes of life being particularly subject to the disease, although for somewhat different reasons. This type of pneumonia is very often the terminal event in aged and feeble persons who have been suffering from chronic disorders, nephritis, diabetes, and cardiac affections. It also occurs in these subjects as a complication of acute maladies, but most often follow the more lengthy and debilitating diseases.

Among the general predisposing factors which may underlie bronchopneumonia is cold, damp, changeable weather. The effect of this is well shown by the greater incidence of the disease in the winter and spring months. Unhygienic surroundings, poor food, insufficient clothing, overcrowded and badly ventilated sleeping quarters, all favor the disease. As a consequence it is more frequent among the poorer classes, is common in the subjects of rickets and other types of malnutrition, and may become almost epidemic in foundling homes and similar institutions. The acute or chronic infections of the respiratory tract, as glanders, leprosy, and anthrax among the less common and tuberculosis as a common form, very frequently induce bronchopneumonia. Possibly in no other disease do lessened powers of resistance of the individual, from whatever cause, play such an important part in determining the inception. This statement is borne out by the wide range of bacteria which under favorable circumstances may serve as exciting agents of the affection.

The bacteriology of bronchopneumonia, in the present state of our knowledge, forms an unsatisfactory chapter. No specific organism has been isolated. The one most frequently present, alone or associated with other bacteria, is the pneumococcus. In Wollstein's series of 100 cases it was present in 67. It was found in 25 of the 33 cases of primary bronchopneumonia, in 15 of them in pure culture. In the 42 cases of the secondary form in which it was present, it was in pure culture in only 10, thus emphasizing the point already made that it is especially active in the primary form of the disease. Wollstein's studies show also that this organism was present in a greater number of those cases in which a large part of one or more lobes was affected as compared with the instances of widely disseminated and smaller foci. Other organisms found in bronchopneumonia are the streptococcus, particularly in those cases following infectious fevers and in aspiration pneumonia, the *Staphylococcus aureus* and *albus*, and Friedländer's bacillus.

In some cases the *Bacillus influenzæ* alone is found. In 131 cases of bronchopneumonia found in the 220 fatal cases of diphtheria studied by Councilman, Mallory, and Pearce, the diphtheria bacillus was third in the list of bacteria recovered from the lung, being exceeded only by the pneumococcus and the streptococcus. Single infections are the exception, mixed infections the rule. When the disease is due to the tubercle bacillus it is best considered simply as pulmonary tuberculosis. With this wide range in the bacterial content of the affected lungs, bronchopneumonia cannot be grouped with the specific infectious diseases, although the bacterial nature of all cases is not to be doubted.

**Morbid Anatomy.**—The affected lung may be slightly increased in size or at least does not collapse so readily as usual or even not at all. On the surface, more commonly posteriorly and in the lower lobes, are dark or bluish depressed areas, usually scattered and small, although occasionally they may include a large part of a lobe. These discolored patches show particularly well in the non-pigmented lungs of children. Between these atelectatic areas the lung exhibited a moderate degree of compensatory emphysema. If the condition be well advanced, slightly projecting solid areas may also be detected. These commonly are not large and may be so small that on first examination the organ appears to crepitate throughout; careful palpation, however, reveals the small, airless foci, presenting on the surface and also scattered through the lung as distinct, although often indifferently defined, nodules. These, although not crepitant, lack the pronounced solidity of the consolidated areas in croupous pneumonia. Over the superficial nodules there is often roughening of the pleura or even a fibrinous exudate, this being more marked in the larger foci. In general, then, the affected part of the lung presents a mottled appearance due to scattered and alternating areas of atelectasis, consolidation, and emphysematous distention. Section of the lung exposes surfaces that are moderately dark red in color, smooth, and bathed with blood or bloody serum or blood-stained mucus. The solidified areas project from the surface to a varying degree, but are never very prominent.

A transverse section of such an area shows the affected bronchus filled with grayish mucus and surrounded by vesicles containing the catarrhal exudate. External to these are the collapsed vesicles of the same or neighboring lobules. Longitudinal section of the pneumonic area shows the racemose arrangement of the bronchus and the infundibula and vesicles filled with the grayish or grayish-yellow, mucoid exudate, some of which can be expressed from the tissue. In some cases these solidified areas are large enough to be excised without obtaining portions containing air, and they then sink in water. In the case of small, widely disseminated foci this test becomes impossible. The intervening collapsed areas are darker in color, smooth, airless, well-defined as separate patches, or, when small in extent, appearing as indistinctly outlined bands passing irregularly between the solidified areas. The bronchi are always more or less inflamed and the peribronchial lymph nodes are usually swollen.

**Morbid Histology.**—In the affected bronchi is an exudate largely mucoid in character, but containing desquamated and fatty epithelial cells and leukocytes, the former being especially prominent. The bronchial wall is infiltrated with leukocytes and shows evidence of marked œdema. Longitudinal sections may reveal irregular or saccular dilatations of the smaller

tubes. The vesicles terminating or surrounding these rhonchi are more or less completely filled with a mucoid and cellular exudate similar to that in the bronchi themselves. Fibrin is rarely found and never in quantities approaching that essentially characteristic of croupous pneumonia. The alveolar and bronchial capillaries are distended, and in the walls of the vesicles are numerous leukocytes, the cellular infiltration of the bronchial and alveolar walls being a conspicuous feature of bronchopneumonia. In many instances the walls of alveoli bordering the solidified areas, and which themselves contain little or no exudate, are occupied by great numbers of leukocytes. In the aspiration and deglutition pneumonias with pus formation, the polynuclear leukocyte predominates and necrotic changes are evident.

The termination of bronchopneumonia in non-fatal cases is usually that of resolution. This process rapidly rids the lung of the non-fibrinous exudate, the bloodvessels and lymphatics caring for that part which is not expectorated. Newly formed epithelium replaces that lost in the desquamative process and the leukocytes and serum in the bronchial and alveolar walls are removed, the affected areas becoming essentially normal. Suppuration frequently terminates the aspiration and deglutition forms of the disease; it is rarely found in the other types. Gangrene occurs in the same kind of cases as does suppuration, occasionally following the latter process. In some instances the disease becomes chronic, the affected areas undergoing fibrosis. This termination is practically restricted to the tuberculous cases, either those tuberculous from the beginning or those upon which tuberculosis is engrafted during the course.

**Symptoms.**—As bronchopneumonia is a disease which arises from the most diverse causes, and as its clinical course depends not only upon the different morbid processes from which it originates and with which it is associated, but also upon the age and previous state of health of the person affected, a comprehensive description applicable to all the forms under which it manifests itself would seem wellnigh impossible. Nevertheless, it is possible to give a general description of its more salient features, afterward discussing its special traits as modified by the causative factors, the extent of the pulmonary involvement, and the age of the patient.

The disease as ordinarily met with in childhood, usually succeeds bronchitis, which, in turn, often depends upon one of the acute infectious diseases, so that, as a rule, symptoms referable to the respiratory organs dominate the clinical picture. The bronchial inflammation is generally present for some time before the lungs become involved, and the disturbances of temperature and respiration incident to the antecedent bronchitis, or the malady upon which the bronchitis depended, have already impaired the patient's health.

The onset, therefore, is not abrupt, but insidious. The temperature ascends gradually, respiration becomes difficult, and the cough grows worse. At the expiration of three or four days after the beginning of the exacerbation, pulmonary involvement has become more pronounced and the constitutional symptoms are considerably accentuated. The patient is very restless and is harassed by dyspnœa and cough. The respirations are short, shallow, and very rapid, varying from fifty to seventy-five or even more per minute. The face may be cyanosed and livid, and well expresses the suffering which the patient experiences for want of air. The alæ nasi dilate with every

breath, and all the auxiliary muscles of respiration are called into play in an effort to force more air into the lungs. This difficulty of respiration may vary in intensity at different times of the day, being worse at night or in the morning, or exacerbations may occur at any time if secretion accumulates or if laryngeal spasm occurs. The cough is more or less severe; it is frequent, hard, and painful, and is accompanied by slight expectoration. In young children there is very little or no expectoration, secretion either being absent or swallowed. The sputum is often blood-stained, but does not have the rusty appearance of that which is coughed up in croupous pneumonia.

The fever varies in severity, and although it may rise as high as 105° it is usually of moderate degree. Pre-agonal elevations of temperature are not uncommon; they may reach as high as 108°. Morning remissions are marked, although vacillations may take place at any time during the day or night. The temperature falls by lysis, which is protracted over several days.

The pulse is very rapid, but its increase in frequency is relatively less than that of the respirations. It is not unusual for it to be as rapid as 140 beats per minute, and it may even become so fast as to be uncountable. The action of the heart becomes weak and irregular and dilatation of the right side may occur.

Anorexia and thirst are always present, and vomiting and diarrhœa are not at all uncommon. The latter may be of toxic origin, or depend upon gastric and intestinal irritation and catarrh resulting from the same exposure to cold that produced the pneumonia. Mucus which has been swallowed may also be vomited.

As regards cutaneous lesions, it is, of course, not uncommon to find the characteristic eruptions of the acute infectious diseases with which bronchopneumonia is associated. The heterogeneous rashes of influenza and diphtheria as well as the typical rash of measles are often encountered. The latter, however, is apt to fade rapidly once the pneumonia is developed. In contradistinction to the regularity with which it appears in croupous pneumonia, herpes labialis is rare.

Cyanosis has already been mentioned. When it is pronounced there is very often an associated coldness and clamminess of the skin. Sweating may also occur early in the disease, but it is of a different character than that occurring in conjunction with marked cyanosis, making the skin warm and moist. For the most part the skin is hot and dry during the early stages, but attacks of sweating sometimes occur.

The urine is scanty, high colored, and contains an abundance of salts. Traces of albumin may be found when the fever is high, and larger quantities are present when such acute infectious diseases as scarlet fever, diphtheria, or influenza have preceded the pulmonary disease.

Pain is not violent, and indeed may be absent. It is not unusual, however, for the patient to complain of dull and occasional shooting pains over the areas of inflammation.

The above clinical picture represents the common form of secondary bronchopneumonia in childhood. Certain variations from this symptom-complex are determined by the extent of the pulmonary lesions, the causative factors of the disease, and the age of the patient. If the foci of consolidation be few in number and scattered throughout the lungs, the symptoms resulting from their presence will not be so severe as those just depicted; the

progress of the disease will be slower, its manifestations more irregular, and its duration longer. If, on the other hand, the pulmonary inflammation be massive in extent and constantly advancing, all the symptoms previously described will be intensified. Dyspnœa may become so violent that the patient will suffocate. This condition has been called "suffocative catarrh."

When bronchopneumonia supervenes upon whooping-cough or tuberculosis, its onset and course are particularly insidious. When it follows whooping-cough its progress as a rule is not attended by very acute symptoms. The child is apathetic and sluggish, refuses food, and gradually loses flesh. Some fever is present, but the cough is not pronounced. The physical signs, too, are not well marked. When complicating measles the temperature ordinarily runs a higher and more constant course than it does in many other forms.

In primary bronchopneumonia, or that developing irrespective of any antecedent bronchitis, the clinical picture is different from the one we have just drawn. The disease is abrupt in onset, and is often ushered in by chills, high fever, and severe nervous phenomena. The temperature is maintained at a higher level, and falls by crisis instead of lysis. The pulmonary symptoms are overbalanced by the constitutional disturbances. The duration, too, is shorter than that of the secondary form. From these remarks it will be seen that primary bronchopneumonia is more closely related to croupous pneumonia than is the secondary form of the disease.

In the aged and infirm the symptoms resulting from disseminated patches of pulmonary consolidation are frequently marked by the manifestations of hypostatic congestion. The development of the disease is not characterized by any pronounced clinical phenomena. Fever, cough, and dyspnœa may all be absent, and the disease first be discovered when physical examination is made. It often happens, too, that the physical signs are not distinct and that proof of the existence of patches of consolidation is first obtained at autopsy. The chronic bronchial catarrh, with which old persons are so frequently affected, may extend to the bronchioles and produce an exudate with resulting areas of consolidation, and when this is the case the increased severity of symptoms is at first often attributed to a mere exacerbation of the bronchial trouble.

Just as the morbid anatomy and symptoms of bronchopneumonia are variable, so likewise is its duration. It may last from a few days to several weeks. In acute suffocative catarrh and that form superimposed upon the chronic bronchitis of the aged, the disease may terminate fatally within forty-eight hours. The course of the disseminated lobular form is progressive, although irregular, exacerbations occurring as new areas of consolidation develop. Its average duration may be said to be from two to three weeks. When developing in cachectic, strumous children it may last for many weeks. It is unusual for any form of bronchopneumonia to terminate in less than ten days.

**Physical Signs.**—From what has already been stated relative to the morbid anatomy and symptomatology of bronchopneumonia, it will be evident that the physical signs must be variable and inconstant.

When only small, isolated, and widely disseminated areas of consolidation exist, percussion will not reveal their presence, and even when considerable consolidation has taken place there may be a sufficient degree of compensatory emphysema to overcome the dulness which otherwise would

be elicited. Indeed, a hyperresonant percussion note is very common. There may, however, be a diminution of normal tympany. It is only when confluence of different consolidated areas takes place, or when the morbid process advances so rapidly as to cause massive consolidation, that marked dulness is detected. It is most common over the bases posteriorly. When this condition is present, retraction of the sternum and lower ribs is frequently observed.

At first auscultation reveals only the signs of bronchitis. Moist and fine subcrepitant rales will be heard over various areas of the thorax, particularly over the bases posteriorly. If there is consolidation of considerable extent, crepitant rales and bronchophony will replace these sounds. The former may, however, be obliterated if the bronchi become filled with secretion. Over the upper anterior and lateral parts of the thorax, impairment of the vesicular murmur, a prolonged expiratory sound and sibilant rales are not uncommon. Very often these different physical manifestations of the disease exist simultaneously in various parts of the thorax, some being present on one side and others on the other; or they may alternate with one another, especially in the protracted forms. It is seen, therefore, that they are extremely fugacious and not in proportion with the severity of the subjective symptoms.

**Complications and Sequelæ.**—Bronchopneumonia may cause complications which materially influence its progress and modify its prognosis.

Of the immediate complications, pleurisy, abscess, and gangrene of the lung, and pulmonary hemorrhage must be considered. The pleura is sometimes affected, but the inflammation is usually fibrinous and confined to localized areas, although it may be general. Effusion rarely occurs, but when it does take place it is apt to be purulent. Abscess and gangrene are not common, although the former probably occurs more frequently than the latter. Often abscesses are minute in size, so that they do not cause serious difficulty. If an abscess ruptures into the pleural cavity, an occurrence which is exceedingly rare, but does happen, pyopneumothorax results. Pepper reported a case in which a consolidated area of lung tissue broke down and opened into the pleural cavity, producing pneumothorax, but such a complication must be exceedingly rare.

Both gangrene and abscess are of more frequent occurrence in those forms of the disease dependent upon acute infections, such as measles, diphtheria, and erysipelas, than in those originating from other causes. Gangrene is often associated with noma, which is to be considered as an expression of the same infection which produced the pneumonia; it is not improbable, moreover, that the gangrenous process itself is due primarily to the same cause instead of being secondary to other lesions in the lung.

The expectoration of blood-stained sputum has already been mentioned; it sometimes happens, especially in suffocative catarrh, that enough blood escapes from the intensely congested pulmonary tissues to constitute a slight hemorrhage. Likewise, where there are confluent or extensive areas of consolidation, small vessels may be eroded and permit the escape of blood. These hemorrhages are not of ill omen.

Cardiac involvements such as endocarditis and pericarditis, as well as otitis media and abscess of the brain, are associated conditions depending upon the same cause as the pneumonia. Convulsions and delirium may occur.

The most important sequel and the one most to be dreaded is tuberculosis. It may affect not only the lungs, but the peritoneum and meninges as well. It must be remembered, however, that bronchopneumonia often develops upon an unsuspected tuberculosis which becomes manifest only as the secondary disease progresses, or is first detected when resolution fails to occur.

**Diagnosis.**—The diagnosis of bronchopneumonia may be easy or difficult according to the manner in which the disease manifests itself. Thus it will be readily made when there is a frank expression of the symptoms which we have mentioned as belonging to the usual secondary form as met with in childhood. This is especially true when there is sufficient consolidation to produce bronchial breathing and bronchophony. On the other hand, when the onset and evolution of the disease are particularly insidious, or for instance when it develops during the course of pertussis or tuberculosis, and when it is complicated with chronic nephritis or the cachectic states of the aged, both symptoms and signs may be so ill-defined as to escape notice. Therefore, it behooves the physician to be constantly on the outlook for evidences of pulmonary involvement ensuing in the course of these diseases. Exacerbations during any acute infectious disease or in convalescence therefrom should also direct his attention to the respiratory organs. In this class of cases, however, it is comparatively easy to detect the supervention of bronchopneumonia.

From acute simple bronchitis it is differentiated by the mildness of the symptoms in the former and by the absence of areas of hyperresonance and dulness in different parts of the chest. In bronchitis, moreover, the rales are coarser than in bronchopneumonia. It would be futile to endeavor to distinguish between capillary bronchitis, so called, and bronchopneumonia, for when the bronchioles are inflamed there is always more or less exudate and consolidation, even although the physical signs pointing to these conditions are obscure or wanting.

From croupous pneumonia, secondary bronchopneumonia is differentiated by the fact that the former attacks persons in good health; that its onset is sudden, severe, and accompanied by a chill; that there is marked prostration in the very beginning of the attack; that the fever is higher and of a continued type, and that it falls by crisis between the fifth and ninth days, most commonly on the seventh; that one lung only is usually affected; that the sputum has a characteristic rusty color; and that herpes labialis is a very constant lesion.

Great difficulty may, however, be experienced in distinguishing between primary bronchopneumonia with diffuse consolidation and genuine croupous pneumonia. The physical signs as related to the consolidated areas are identical in the two diseases, although in bronchopneumonia it is common to find signs of localized areas of disease in other portions of the chest. The character of the sputum in the two maladies constitutes a valuable differential sign, but one which cannot be made use of in children for the reason that secretion is absent or is swallowed instead of being expectorated. It not uncommonly happens that diagnosis is first made when the temperature falls by crisis between the fifth and ninth day of the illness.

There is a decided similarity between the insidious, subacute forms of bronchopneumonia and tuberculosis. The most valuable means of distinguishing between the two is by examination of the sputum. In suspected

cases in which repeated examinations prove negative an injection of tuberculin may be given, provided, of course, that the temperature has fallen to normal. Small areas of tuberculous consolidation in the apices, together with the associated congestion of contiguous areas, may give rise to subcrepitant rales, and the hectic fever may also resemble the intermittent type of that occurring in bronchopneumonia.

Careful inquiry into the family and personal history of the patient, together with a thorough physical examination and search for signs of tuberculosis in other parts of the body, will do much to help the physician in making a correct diagnosis.

Pulmonary congestion occurring in childhood is more sudden in onset and of shorter duration than bronchopneumonia. The temperature is higher and the disease is generally confined to one lung.

Small pleural effusions giving rise to crepitant rales heard at the upper boundary of the effusion when a deep inspiration is taken may simulate an insidious bronchopneumonia. Exploratory puncture will clear up any doubt which cannot be overcome by thorough investigation of other signs and symptoms.

**Prognosis.**—The same factors which determine the clinical course of bronchopneumonia make its prognosis variable, but the disease is always serious. First the age of the patient must be considered. At the two extremes of life the mortality is particularly high. In children there is a definite relation between age and mortality; the younger the patients the higher the death rate. Probably from 30 to 50 per cent. of all cases occurring in childhood terminate fatally. In old age, too, the mortality is exceedingly high.

The previous health of the patient and also his surroundings contribute not a little in determining the degree of resistance which he can assert in combating the disease. All conditions of faulty nutrition, all weakening influences, such as want of fresh air and sunlight, and proper attention to personal hygiene, as well as such constitutional defects as rickets and scrofulosis, render the prognosis less favorable. Children who are crowded in almshouses, asylums, and charity hospitals do not do so well as they who are more favorably situated.

The immediate cause of the disease also exerts a material influence upon prognosis. Thus the disease is especially fatal when it occurs in the course of variola, diphtheria, erysipelas, and measles, as well as when it ensues as a complication of tuberculosis.

Prognosis is also modified by the extent of the pulmonary inflammation. It is evident that the symptoms will be more severe and the chances of recovery less when there is massive involvement of the lungs than when there are only a few widely disseminated areas of consolidation. Among the symptoms which augur ill are marked cyanosis, cardiac failure, Cheyne-Stokes breathing, sudden fall of temperature, hyperpyrexia, delirium, convulsions, and stupor. Pulmonary abscess, unless very minute in size, decidedly increases the danger of death, while pulmonary gangrene is always fatal.

Convalescence is slow and recurrences are common. In primary bronchopneumonia the mortality is not high and recovery is rapid.

**Prophylaxis and Treatment.**—Much can be done by adequate prophylaxis to reduce the frequency of this disease. As it is of infectious

origin, and as the infection may be either endogenous or exogenous, measures directed both to the proper hygienic care of those not diseased and to isolation of the sick will be of use in lowering its occurrence. As concerns individual prophylaxis, the rules of personal hygiene should be strictly observed. Fresh air, sunlight, nutritious food, proper clothing, regular bathing, and sufficient sleep all combine to increase the power of vital resistance.

Since microörganisms potent in the production of this disease are known to inhabit the mouth, special attention should be given to buccal hygiene. Careful and regular cleansing of the teeth, together with the use of antiseptic mouth washes, must be insisted upon. The latter are especially important for those predisposed to diseases of the respiratory organs. Disease of the nasal cavities, pharynx, and tonsils must not be neglected, but receive prompt and skilful treatment. Exposure to dampness and cold must be avoided. Persons predisposed to pulmonary disease should be sedulously excluded from those suffering with pneumonia or bronchopneumonia.

As great a degree of isolation of the sick as is compatible with our existing social conditions and present hospital facilities should be practised. An ideal method would be to care for a small number of patients in large, well-ventilated pavilions, thereby doing away with the disadvantages of overcrowding and at the same time securing adequate isolation. Departments in hospitals for contagious diseases might be reserved for patients who develop pneumonia. No doubt its frequency as a complication of the acute infectious fevers, affecting large numbers of children in special hospitals, would be somewhat diminished if this method could be adopted, as it would remove the additional risk of contact with those already having the disease. The execution of these ideas, however, would require concerted action on the part of physicians, philanthropists, and legislators, an action which unfortunately is not likely to be taken for some time to come.

In regard to prophylaxis in the aged and infirm the above rules of hygiene also apply. In addition thereto it is important to prevent this class of persons, whenever possible, from maintaining the dorsal decubitus for long periods of time.

Much can be done, too, to prevent the supervention of bronchopneumonia in convalescence from acute diseases. For this purpose warm clothing and avoidance of exposure to cold are of the utmost importance. The use of antiseptic mouth washes should, of course, never be omitted. The child should never be allowed to lie for any length of time in the same position, especially the dorsal, but should be turned from one side to the other at short intervals. No case of bronchitis in a child should be regarded as a trivial affection and one not demanding careful observation and treatment. On the contrary, it ought always to be borne in mind that the inflammation may extend from the large bronchi to the bronchioles, and produce exudative inflammation in the lung. For this reason active treatment should be instituted.

When bronchopneumonia has actually developed the patient should be placed in a warm, well-ventilated, and well-lighted room, preferably one which is heated by means of an open fireplace. The hot, dry, and not infrequently dust-laden air of rooms supplied with furnace heat is very

irritating to the respiratory tract and serves both to make the patient uncomfortable and increase the severity of his disease. It will be found that steam, either natural or medicated, diffused from a bronchitis kettle will keep the air of the room moist and makes the patient's breathing easier. If medicated steam is desired, a few grains of menthol or a half dram of tincture of benzoin may be added to the water. It is hardly necessary to state that exposure to draughts must be avoided and that the temperature of the room must be kept equable.

Our therapeutic efforts must be directed to sustaining the patient's strength, to combating toxæmia, and to limiting the extent of the pulmonary lesions.

For the first purpose nutritious, easily digestible food, together with the judicious use of stimulants, is of the highest importance. Milk, koumyss, meat juice, strong broths, and cocoa are suitable articles of diet. Milk holds first rank, but the others may be given alternately with it for the purpose of preventing the patient from becoming tired of an unvaried dietary. All food should be given in small quantity every two or three hours.

Hydrotherapeutic measures, and heat and cold are among our most valuable resources in combating this disease. Cool sponging will reduce temperature, lessen toxæmia, and allay restlessness. For the same purpose a full bath of moderate temperature, for instance 85° to 90°, may sometimes be advantageously employed for young children who can be easily lifted from the bed and placed in a bath-tub. Its duration should be from five to ten minutes and it should be accompanied by friction of the surface. Cold affusions will often cause a child suffering with bronchial obstruction to rally and expel the mucus which is oppressing the breathing. The crying and agitation produced by the shock of the cold water has a most beneficial effect. The water used for this purpose should be at a temperature varying from 70° to 60°. An alternate hot and cold plunge may also be employed for this purpose. It should be used only in desperate cases and then not be repeated too often.

The cold compress to the chest has been strongly recommended. It is made by taking three or four layers of linen, dipping them into water, and then applying them closely around the body from the clavicle above to the umbilicus below. They are then to be covered with a heavy layer of flannel. If the temperature is very high the compress should not be wrung out quite dry, as by leaving more water in it the action will be more protracted and more heat will be abstracted. The compress should be changed every half-hour. An ice-bag to the head will diminish cerebral congestion, lower temperature and relieve pain. It is important to have an ice-bag that does not leak. Saline infusions are valuable for raising blood pressure, overcoming toxæmia, and stimulating the nervous system; not more than 250 cc. of solution should be given to children. If used for infants 50 cc. is quite enough.

Drugs are to be used first of all to maintain the patient's strength and meet symptoms which arise as the disease progresses. In the beginning of an attack it is advisable to administer a dose of calomel to clear out the intestines. From one-half to one grain may be given in divided doses to infants and young children; to older children and adults two or three grains administered in the same manner is not too much. It is well to give enough not only to produce free catharsis, but also to stimulate the kidneys to activity.

The most valuable drugs in the treatment of bronchopneumonia are the stimulants, and of these alcohol holds first place. In those forms originating from the acute infections it is particularly valuable, not only as a stimulant, but likewise combating toxæmia to a marked degree. In such cases it should be pushed to its physiological limit. Even young children can consume a considerable quantity in twenty-four hours without manifesting any toxic effects. Infants less than a year old can take ten or fifteen drops of brandy or whisky in a little water every hour and older children can take from one-half to one dram according to their age. In these cases the drug should be given from the very beginning of the disease. There are few cases, irrespective of their origin, in which alcohol is not indicated.

An old brandy or mature whisky is as a rule the best preparation to use; if the stomach rebels against them champagne may be substituted. Other stimulants of value are Hoffman's anodyne, aromatic spirit of ammonia, and carbonate of ammonia.

When the breathing is labored and cyanosis marked, from fifteen drops to a teaspoonful of Hoffman's anodyne, according to the age of the patient, will often afford relief and improve the color. Aromatic spirit of ammonia in like dose may be used for the same purpose.

Carbonate of ammonia, gr. 1 to 5 (0.06 to 0.3 gm.), every two or three hours, acts both as a stimulant and an expectorant; it must be well diluted and preferably mixed with a little elixir of orange or syrup of acacia.

When the lungs and bronchi are rapidly filling with mucus, a dose of atropine will often arrest the secretion and tide the patient over a critical period. From gr. $\frac{1}{500}$ to $\frac{1}{100}$ (0.0001 to 0.0006 gm.) may be given. The atropine may be preceded by an emetic dose of ipecacuanha or apomorphine, which will frequently result in the expulsion of a large quantity of mucus. A moderate dose of strychnine may be combined with the atropine, if desired for its action as a respiratory stimulant.

Ether and camphor, given hypodermically, are indicated in severe heart failure. Inhalations of oxygen relieve dyspnœa and lessen cyanosis.

Expectorants are serviceable. Ipecacuanha during the early stages of the disease, and ammonium chloride and senega during the later stages are the ones most likely to prove of value.

When racking, painful cough is present, narcotics must be resorted to. They may be given separately or in combination with the other remedies employed. For young children paregoric is probably the safest; for those who are older small doses of codeine or heroine may be given with safety, from gr. $\frac{1}{2}$ to $\frac{1}{8}$ (0.03 to 0.008 gm.) of the former and from gr. $\frac{1}{40}$ to $\frac{1}{20}$ (0.0015 to 0.003 gm.) of the latter being administered every three or four hours. During convalescence tonics, such as iodide of iron, arsenic, and cod-liver oil, are indicated. Residence in a warm, dry, southern climate in winter and in the mountains or at the sea-shore in summer will materially accelerate complete restoration to health.

## CIRRHOSIS OF THE LUNGS.

**Etiology.**—Under the names pulmonary cirrhosis, or, the better term, pulmonary sclerosis, interstitial pneumonia, chronic interstitial pneumonia, fibroid lung, and fibroid pneumonia, is included a condition of the lung which

in general is quite definite, but which in its manifestations is so variable that satisfactory classification is impossible. This is due to the fact that every inflammatory lesion in that organ may result in the formation of new fibrous tissue and a majority of them always so terminate. The affection, then, is essentially secondary in character and any etiological division must be based on diverse causative factors. Any classification adopted therefore answers rather to convenience than to scientific accuracy. Certain types of pulmonary sclerosis, however, are predominantly local in origin and development, while others are more diffuse in character.

The localized form of sclerosis is that which develops around or in the lesions of focal diseases of the lung, as gummas, abscesses, infarcts, tumors, and parasitic cysts. Small collections of pigment may result in sclerosed patches in the apices, but commonly this material produces a diffuse fibrosis. The apex also is the common site of local fibroid tuberculosis, a large majority of adults coming to postmortem possessing small foci of this character in one or both lungs. In many instances such lesion is only a wrinkled, band-like area of fibroid lung beneath a patch of thickened pleura. Other chronic infections, as actinomycosis, glanders, and leprosy, may induce localized pulmonary fibrosis.

Diffuse chronic interstitial pneumonia is the result of several pathological processes. Croupous pneumonia occasionally terminates in this manner. For some unexplained reason, possibly the non-production of autolysins, resolution does not occur and the fibrinous exudate collected in the vesicles during the stage of red hepatization is substituted by fibrous tissue. The connective-tissue formation necessarily begins in the alveolar walls, as from this source must be derived the new vessels which appear in the intravesicular new formation. It is held by some, however, that the new tissue is actually formed from the leukocytes in the vesicles rather than from the cells derived from proliferation of connective-tissue elements in the walls themselves. Proliferative changes in the alveolar epithelium may for a time be active during this transformation of the exudate, but eventually the new tissue within the vesicles merges with the thickened, enclosing walls, which take a relatively inactive part in the process, and the area becomes entirely fibroid. Usually this lesion is patchy in distribution, but the parenchyma of an entire lobe may be thus obliterated. To the condition is given the name organizing or organized croupous pneumonia or simply the term chronic pneumonia. The last is preferred by some observers who regard the process as practically distinct from the very beginning, in other words, a primary chronic pneumonia rather than an atypical form of the croupous variety. It is by these clinicians said to be more common in debilitated persons; predisposing causes are extreme and long-maintained reduction in temperature and preceding hyperplastic changes in the pleura. Marchand suggests the name chronic fibrous pneumonia.

A second type of diffuse sclerosis is that known as pleurogenous interstitial pneumonia. As the name implies, the process follows inflammation of the pleura, generally the plastic type. From the thickened pleura the connective-tissue increase extends into the lung, affecting first the interlobular septa and second the finer fibrous structure of the organ. This process is by some not regarded as a distinct type of fibroid pneumonia, but in origin it differs materially from certain cases in which the lesion in the lung is very similar, that is, the fibrosis which develops in a lung that has long been

compressed by pleural exudate and thereby largely rendered functionless. Here the pleura is also thickened, but there are no adhesions and the pulmonary fibrosis is secondary to the collapse and is general throughout the organ. In the pleurogenous variety the greatly thickened pleura is nearly always firmly adherent to the chest wall and the fibroid areas in the lung can be traced directly downward from the pleura.

Chronic interstitial pneumonia due to the inhalation of dust, whether derived from coal, iron, stone, or other sources, is a relatively common affection elsewhere considered under the heading of Pneumokoniosis. The fibrosis is due directly to the chronic irritation of the foreign particles in the tissues, the degree depending upon the amount and character of the inhaled material. Somewhat analogous is the connective-tissue production in chronic congestion of the lung, which is induced by the co-existing venous stasis and the blood pigment deposited in the tissues; this has been discussed as brown induration. Another cause of pulmonary sclerosis is pressure exerted upon the lung by neighboring structures, as new-growths and diverticula of the œsophagus, tumors of the mediastinum, and aneurism of the large thoracic vessels. Pulmonary fibrosis due to syphilis is found in the lungs of the newborn as the so-called white hepatization, due to thickening of the alveolar walls, or in the adult as a diffuse process beginning usually at the root of the lung and extending outward toward the pleura. At times this syphilitic fibrosis appears to extend from the pleura inward. In either case it represents better than any other of the types mentioned a primary, uncomplicated sclerosis of the lung. Bronchopneumonia may terminate atypically in fibroid changes in some of the involved lobules. In these cases the fibrosis begins as a chronic bronchitis or peribronchitis, invading later the surrounding parenchyma.

**Morbid Anatomy.**—This varies as does the etiology. In the disseminated forms, which may be bilateral, the affected lung in part or as a whole is more firm than the normal organ and cuts with increased resistance. The fibroid areas, which may be seen through the pleura, present on the cut surface as grayish masses, distinctly circumscribed or radiating from the bronchi as more or less prominent bands marking the interlobar or interlobular septa. These areas are more frequent in the lower lobes and are commonly pigmented. If they are multiple and extensive the intervening lung is emphysematous. The bronchi not infrequently show moderate dilatation. The organ on removal or incision may show little or no tendency to collapse.

The massive type of pulmonary sclerosis differs from the preceding chiefly in degree. It is necessarily unilateral and while it may affect only a lobe it usually involves an entire lung. The chest wall over the affected organ is less prominent than normal; it may be distinctly sunken, with resulting depression of the shoulder of that side. The heart, which is commonly hypertrophied, and the attached tissues are drawn far to the diseased side, their usual site being occupied by the opposite lung, which is emphysematous, often to an extreme degree. The pleura over the fibroid lung may or may not be conspicuously thickened. In the cases of pleurogenous pneumonia it is very thick and united to the chest wall by adhesions so dense as to be cut with difficulty when removing the organ. When universal pleural adhesions are absent the lung itself may be extremely small, not larger than a fist, and is drawn inward and backward close to the spinal column. It is

firm, cuts with great difficulty, and may be airless and doughy to the touch. The incised surfaces are largely gray in color, owing to the great amount of fibrous tissue surrounding the bronchi and bloodvessels. The former structures are usually dilated at times to such a marked degree that the bronchiectatic cavities are the most conspicuous features of the specimen. Evidence of infection is not uncommonly present; this may be pyogenic or tuberculous, more often the latter, and is occasionally manifested by cavity formation. Tuberculosis is often microscopically demonstrable when there is no gross evidence of the disease. In such cases the opposite lung also is usually tuberculous. In the residual parenchyma of the sclerosed lung there is constantly evidence of acute or chronic catarrhal inflammation.

**Symptoms.**—The changes in the lung may be well advanced before any symptoms other than those of chronic bronchitis, together with slight shortness of breath upon exertion, manifest themselves. The patient may have had a cough of varying intensity for years, being better in summer and worse in winter, but his health has never been seriously impaired. As the sclerosis becomes more extensive, however, and the circulatory area of the lung is progressively diminished the resulting interference with aëration of the blood will give rise to more constant difficulty of breathing than was formerly experienced; the concomitant destruction of elastic tissue will likewise contribute to the production of dyspnœa.

As a result of these changes in the lung an abnormal amount of work is thrown upon the right side of the heart, which hypertrophies in an attempt to sustain the burden placed upon it. In course of time, however, compensation may fail, and the symptoms of rupture will then be superimposed upon those produced by the pulmonary lesions. As the heart fails gradually instead of rapidly the access of cardiac symptoms will naturally be slow. The cough and dyspnœa become worse, the patient loses strength and becomes emaciated, may show signs of cyanosis, and in the advanced stages of his malady may become dropsical.

Cough varies with the stage of the disease and the nature of the pulmonary lesions. As already stated it is an early symptom, varies with the season, and becomes progressively worse as the disease advances. If the bronchi are dilated, a condition not at all uncommon, especially when the disease develops as a sequel to bronchopneumonia, the cough assumes a paroxysmal type owing to the effort necessary to force the secretion from the cavities in which it has collected. Under these circumstances it is often worse in the morning than at other times. Retained secretions may undergo decomposition and give rise to hectic fever, which, however, is not of intense degree, the temperature rarely rising higher than 102°. Fever may also be the sign of a superimposed tuberculous infection.

In the early stages there is nothing characteristic about the sputum, unless perchance the primary cause is some form of pneumokoniosis, in which case it will be stained by one of the pigments present in this latter affection. When there is bronchiectasis the sputum is especially profuse and of a muco-purulent character. If the sputum be retained long in a cavity or if the walls of the cavity ulcerate it may become very offensive, and may be blood-stained if minute vessels in the walls of the cavity are eroded. Blood may also be present after failure of the right side of the heart.

**Physical Signs.**—When cirrhosis of the lung is at all extensive it is accompanied by marked changes in the configuration of the thorax. The contrac-

tion and retraction of the lung produce a space in the cavity of the chest, between the surface of the lung and the internal aspect of the thoracic wall, as a result of which the wall retracts. This retraction is particularly marked when there are extensive pleural adhesions. As a rule, the greatest degree of retraction is observed anteriorly between the clavicle and the sixth rib, and posteriorly below the angle of the scapula. The shoulders droop; the intercostal spaces are narrowed; the lateral thoracic wall loses its normal arch, being angular instead of rounded; the apex of the sternum is pulled to one side, and the spine deviates laterally. The respiratory movements are diminished on the affected side. The position of the heart is also altered. When the left lung is affected the apex beat will be displaced upward and outward. Owing to retraction of the anterior border of the lung the pulsation of the pulmonary artery may be revealed in the second intercostal space. When the right lung is affected the heart will be pulled downward and to the right; displacement may be so marked that the condition may strongly resemble congenital dextrocardia.

Palpation often shows that tactile fremitus is increased. Upon percussion various notes will be elicited. Over the areas of cirrhosis, normal resonance is diminished, or perhaps dulness may be present, especially if the area is large and superficially situated. Areas of compensatory emphysema give a hyperresonance or sonorous sound, while bronchiectatic cavities may emit an amphoric note. When the cirrhotic process affects the right lung the liver ascends and the area of hepatic dulness extends higher than normal, and perhaps may be continuous with pulmonary dulness. On the other hand, when the left lung is contracted, the stomach and intestines ascend, with the result that tympany is heard over the lower portion of the thorax, dulness or impaired resonance being confined to the superior portion of the chest.

The results of auscultation are not distinctive. The vesicular murmur is diminished and bronchial breathing may be detected if there is an extensive area of cirrhosed lung. Over a bronchiectatic cavity amphoric breathing may be heard. Rales and rhonchi of various kinds will be present during the different stages of the disease, as well as when exacerbations occur.

These in general are the physical signs met with in the different forms and various stages of the disease. Their presence depends in part upon the cause of the pulmonary lesion. Thus, dilatation of the bronchi and its accompanying signs are more common when sclerosis develops after bronchopneumonia, deformity of the thorax more pronounced when it occurs as the result of pleurisy with adhesions, and the area of impaired resonance more sharply limited when it follows an unresolved croupous pneumonia. These, however, are only minor differences.

**Complications.**—Softening of the indurated areas may occur, or tuberculosis be superimposed upon the sclerotic (or softened) areas. Bronchiectasis and cardiac changes have already been considered.

**Diagnosis.**—In well-developed cases of cirrhosis of the lung in which an accurate history of the development of the disease is obtainable, diagnosis may be made at once with reasonable certainty. In other cases it may be very difficult. The diseases from which it must be distinguished are chronic pleurisy with retraction of the lung, new-growths, syphilis, and tuberculosis.

In pleurisy with retraction the deformity of the thorax is more irregular than in diffuse cirrhosis of the lung, and the lower portions of the lung are

the parts most likely to be affected, whereas in cirrhosis the upper lobes are commonly the site of the disease. Moreover, in pleurisy bronchial breathing is not present, although the breath sounds may be weak or even inaudible.

Hæmoptysis, although of not uncommon occurrence in cirrhosis associated with bronchiectasis, does not occur in pleurisy.

Tumors of the lung and costal pleura often produce contraction and retraction of the lung. Owing to the pressure which they exert and also to the interference which they cause with the ingress of air into the lung, the alveoli collapse, with the result that symptoms and signs similar to many observed in cirrhosis manifest themselves. Under these circumstances differential diagnosis may at first be very difficult, particularly in the absence of an adequate history. In case the growth is malignant, involvement of the neighboring lymph glands, signs of mediastinal compression, and the cachexia peculiar to malignant disease will be the greatest helps in enabling one to form a correct diagnosis. The history of the case, provided that an intelligent and authentic account can be obtained, will also be of great value, particularly information relative to the mode of onset and evolution of the disease. Syphilis may produce sclerosis of the lung, giving rise to symptoms exactly the same as those found in other forms of the disease, and unless a syphilitic history can be obtained, or signs of syphilis found in other parts of the body, no definite knowledge can be had in regard to the origin of the pulmonary disorder. Of course, in the absence of other causes, syphilis might be suspected.

The discrimination between beginning sclerosis and incipient tuberculosis may present many difficulties. Given a patient who has had an attack of croupous pneumonia from which he has never fully recovered, with more or less persistent cough, some difficulty of respiration as time elapsed, perhaps slight elevations of temperature, and presenting, moreover, such physical signs as areas of consolidation, exaggeration of vocal fremitus, and diminution of normal breath sounds, the question which arises is whether he has pulmonary tuberculosis or is beginning to feel the effects of a sclerotic process in the lung. Unless the tubercle bacillus can be found in the sputum, time alone can decide this question.

Tuberculosis may also be superimposed upon cirrhosis of the lung, and in cases of long-standing in which bronchiectatic cavities exist and hectic fever is present, its association may not be suspected unless perchance examination of the sputum reveals the tubercle bacillus. In fibroid phthisis the deformity characteristic of advanced sclerosis is absent, although in the former disease there is often some flattening of the infraclavicular spaces. The symptoms and signs of the two affections are very similar, and in the earlier stages one may easily be confounded with the other.

**Prognosis.**—Cirrhosis of the lung is of course incurable, but, as already stated, its progress may be so slow as not to interfere materially with health for many years. This is especially true of the pleurogenous form.

When the disease develops after pneumonia, either lobar or lobular, its course is not so protracted as when it follows pleurisy. Tuberculosis is frequently superimposed upon lobar sclerosis within a short time of the beginning of the malady, and dilatation of the bronchi is often associated with the lobular form. Both these conditions contribute to the severity of the disease and tend to shorten the duration of life. Cardiac complications may cause death in the more advanced cases.

**Treatment.**—It is evident from what has already been stated that cirrhosis of the lung is an incurable malady. For this reason attempts to prevent it should be made with all the greater assiduity. As the disease is known to develop after incompletely resolved pneumonia, no pains should be spared to secure resolution in every case. For this purpose blisters or other forms of counterirritation to the chest, respiratory gymnastics, residence in a warm, equable climate, together with the internal administration of such drugs as cod-liver oil, arsenic, syrup of hydriodic acid, or iodide of iron are the measures which naturally suggest themselves as being appropriate.

Hygienic measures are of the utmost importance in the management. If the patient's means will permit, he should reside in a warm climate where variations of temperature do not prevail, and where there is not much alteration in the degree of humidity. If secretion be profuse, a dry climate, like that of Arizona, for instance, is suitable. High altitudes are of course contra-indicated for persons in the advanced stages of the disease when cardiac complications are present. It is important, too, that the air shall be pure and free from dust. Those who cannot change their residence at will should at least endeavor to obtain as much fresh air and sunshine as they can, and to relinquish occupations entailing the inhalation of dust-laden air. They should remain indoors in inclement weather, and should be warmly clad. It is important to maintain bodily nutrition at the highest possible level, and to secure this end a generous diet should be provided. Milk and eggs may be taken between meals, and cocoa and crackers or a slice of toasted bread may be taken before retiring. Highly seasoned, rich and indigestible food must not be eaten. Tobacco must be interdicted and no alcoholic beverages, other than a glass or two of burgundy or claret at dinner, or a glass of ale with luncheon, should be allowed.

The tonic hydrotherapeutic measures, such as the half bath of moderate temperature in conjunction with sprinkling of the breast and back with cool water, and later, as the patient becomes more accustomed to the treatment, the use of cool or cold affusions are of decided value in improving nutrition and lessening the liability to contract cold.

As regards treatment by drugs the early stages of the disease are best managed by the employment of stimulating expectorants for the bronchitis, such as benzoate of ammonium, in 10-grain doses (0.6 gm.) given in capsules after meals, or 5 minims of oil of sandal (0.3 cc.) administered in the same manner. If secretion is profuse, terpin hydrate may be employed instead. Small doses of codeine or heroine may be necessary to alleviate the cough. For acute exacerbations of the bronchitis, ipecacuanha or carbonate of ammonium will be found useful. Inhalations of turpentine or carbolic acid may be advantageously employed when bronchiectatic cavities are present. Digitalis must be used according to the usual rules when cardiac compensation begins to fail.

## PNEUMOKONIOSIS.

**Etiology.**—Pneumokoniosis is an affection of the lungs developing in those who habitually inspire excessively dust-laden air and is therefore to be classed with the occupation diseases. Chief among the varieties in fre-

quency is anthracosis, due to the inhalation of coal-dust. Siderosis is applied to the condition when particles of iron are inhaled, as in the cases of metal-grinders and nail-makers; in the former more or less stone-dust is almost always associated with the iron. In those who work with stone the affection is known as lithosis or chalicosis. Kaolinosis, or clay-workers' disease, has been described and a similar infiltration of the lung occurs in those who handle grain, in those employed in mills dealing with cotton, shoddy, and like materials, and to a lesser degree in street-sweepers and others of similar occupation. From the origin of the condition and its associated lesions, many colloquial names have been derived, as coal-miners' disease, grinders' rot, and miners' or nailers' or stone-cutters' phthisis.

Much of the dust inhaled by all inhabitants of cities does not reach the pulmonary tissues, being returned by the combined action of the secretions and the ciliated cells of the respiratory tract. When the inspired dust is in excess of this protective capacity, as in the occupations named, it passes into and through the alveolar epithelial cells and also those of the finer bronchi and finally reaches the connective tissue beneath. A small part is there retained, the remainder being carried by phagocytes into the lymph stream, by which it is distributed throughout the lung. The researches of Arnold, Hamilton, and others have shown that it is deposited especially in the subpleural interlobular septa, in the peribronchial lymph nodes, and in the perivascular lymph spaces of the alveolar walls. When the process becomes extensive, the substernal and tracheal lymph nodes also become infiltrated with the pigment.

**Morbid Anatomy.**—This depends to a large extent upon the quantity and character of the inhaled material, although in general the lesions caused by all are much the same. Of these changes the most conspicuous is an increase of fibrous tissue, either localized or diffuse in type. As this change is the result of irritation by the infiltrated pigment, the degree and extent of the fibrosis vary proportionately with those of the former. The posterior and middle parts of the lung are chiefly affected, especially in moderate degrees of the disease, although some types, particularly anthracosis, may be more prominent in the apices. The anthracotic lung ranges in color from a mottled appearance, due to variously sized dark patches beneath the pleura and scattered over the cut surfaces, to an organ that is almost uniformly slaty or even coal-black. From the cut surface of a lung showing the extreme type of the infiltration may in some instances be expressed an ink-colored fluid. In the organs that are not so extremely black, areas variable in size which are gray or grayish black in color, and which are firm and cut with resistance, may be clearly seen on the incised surfaces. These are portions of the lung which have become largely or entirely fibroid, the exact color depending upon the amount of pigment contained within the sclerosed area. Often these areas are in the form of band-like masses extending inward from the thickened pleura or they may be more marked toward the root of the lung.

The affected organ in some instances is very dark and yet crepitates throughout, but in most cases sections that are quite airless are readily found. These are occasionally so large as to include the greater part of a lobe or of a lung, Osler finding in one specimen a fibroid area 18 by 6 by 4.5 cm. in size. The condition is essentially a chronic interstitial pneumonia, although, as pointed out by some writers, from the general location of the pigment

which induces the process it is in origin rather a bilateral chronic productive peribronchitis. The peribronchial lymph nodes are enlarged, firm, and on section show mottled or uniformly dark surfaces. In marked cases the mediastinal lymph nodes also are enlarged, some of them enormously so, and are grayish black in color.

Microscopically, in addition to the increased fibrous tissue, an accompanying catarrhal inflammation can be detected, the epithelium of the alveoli and the smaller bronchioles being granular, pigmented, and desquamating. These pigment-bearing cells are often found in the sputum in large numbers. The denudation of the epithelium reduces the protective powers of the lung against bacteria, and infection is thus rendered more probable, although in at least some instances this exposure appears to be partly or entirely counterbalanced by the presence of the coal-dust, probably aided by the sclerosis. Statistics of a number of observers have been thought to indicate that coal-dust actually militates against the colonization of the tubercle bacillus in the lung, or at least that coal-miners are infected less often than are other individuals. Wainwright, in a study of tuberculosis in the anthracite regions of Pennsylvania, found that the deaths from that disease for ten years at Scranton were 3.37 per cent. for adult mine-workers and 9.97 per cent. for those in all other occupations. Many of the small areas of softening in anthracotic lungs are non-tuberculous and may even be non-bacterial in origin.

Pneumokoniosis due to materials other than coal-dust presents lesions that are in many points similar to those described. Catarrhal inflammation of the parenchyma and hyperplasia of the connective tissue of the lung occurs. In the case of stone-dust the particles tend to form nodules of various sizes which are gray or dark in color or even give a yellowish tint to the lung, this depending upon the type of the deposited material. These nodules are often exceedingly hard, gritty to the knife, or impossible to section. The surrounding tissue may soften, leaving the concretion in a cavity. If small these pneumoliths may be expectorated. The oxides of iron give a reddish color to the lung.

Associated pulmonary lesions of any of the types of pneumokoniosis include chronic bronchitis, bronchiectasis and emphysema. The first named is really a part of the condition itself and often gives rise to the most prominent symptoms of the disease. Enlarged and pigmented bronchial lymph nodes may become adherent to the œsophagus and by softening finally rupture into that structure. The blood stream is in some instances entered by the pigment from peribronchial lymph nodes which adhere to and finally rupture into contiguous veins. In these cases the pigment is deposited in the liver and other viscera and may appear in the urine.

**Symptoms.**—Pneumokoniosis may persist for years without causing impairment of health, and in cases where it is not of long standing all signs of it may subside in a short time if the exciting cause is removed. As a rule the first symptoms complained of are those of chronic bronchitis. The cough varies in intensity. The sputum is usually scanty, although in some cases it is abundant. It is variously colored according to the nature of the dust which has been inhaled. In anthracosis it is black, in siderosis red, owing to the presence of iron oxide.

As more and more pigment is deposited in the lung, the pulmonary circulation is interfered with, so that signs of emphysema may develop.

Reactive inflammation is also often produced by the irritating effects of the foreign substance, the connective tissue proliferating and then contracting, with the result that sclerosis takes place. In either case cough will be intensified, dyspnœa appear, and progressive loss of flesh and strength ensue. Tuberculous infection may take place and cavities form, which may go on to ulceration, giving rise to the phenomena of septic infection.

There is nothing distinctive about the physical signs. At first they are those of chronic bronchitis, and later those of emphysema, cirrhosis of the lung, or cavity.

**Diagnosis.**—The diagnosis is to be made by the history of the case, the character of the sputum, and the signs of the conditions which develop as the result of the foreign particles in the lung.

**Prognosis.**—The prognosis varies with the extent of the lesions and the possibility of removing the patient from the causative influences. In the stage of chronic bronchitis it is good if the cause can be removed. In the later stages, also, improvement will usually follow removal from exposure to the exciting factors, but when emphysema is once fully established there is, of course, no hope of complete recovery.

It seems probable to the writer that the unhygienic surroundings under which many of the people who are affected with pneumokoniosis live, as well as the excessive use of alcohol to which some of them are addicted, contribute in considerable measure to the supervention of the later stages of their disease, and that if these factors could be eliminated they might pursue their vocations for a longer period without their health undergoing any material degeneration. That the amount of dust inhaled exerts a decided influence upon the rapidity with which the disease becomes serious is well illustrated by Moritz's investigations among the grinders at Solingen, Germany. He found that there were no fork-grinders over forty years of age, while of the total number of knife-grinders 5.5 per cent. were above forty. The fork-grinders work with dry stones, the knife-grinders with moist. Of the scissors-grinders 8.4 per cent. lived to be more than forty. They, too, work with moist stones, the same as the knife-grinders, but they sit farther away from the stones than do the latter and therefore inhale less dust.

**Treatment.**—Prophylaxis is of greater importance than treatment. The proper ventilation of workshops where the air is laden with dust should be secured, and provision made in mines for the escape of contaminated air through flues. Workmen should be compelled to wear respirators, and should be urged to take as much exercise in the open air as is possible. If all of them could be induced, and did their means permit them, to live in hygienic surroundings the effect no doubt would be most salutary. In this respect, however, the most that the physician can do is to offer advice to individuals in regard to the importance of keeping the windows of sleeping-rooms open, reducing the temperature of the usually overheated living-rooms, the necessity of personal cleanliness, and of the harm which is bound to result from the abuse of alcoholic beverages. As our social conditions improve, as the masses become more intelligent, and the few more humane, the frequency of this as well as of other affections due to unhygienic surroundings will decrease.

In regard to medical treatment the indications to be met will depend upon the stage of the disease. For chronic bronchitis the stimulants, such as

ammonium chloride, oil of sandalwood, or of eucalyptus, may be employed, either singly or in combination with some preparation of opium. Inhalations of menthol and eucalyptol may also afford some relief. Tonics, too, such as the simple bitters or small doses of quinine and iron, may help to maintain nutrition. In the latter stages, when emphysema has developed, the measures recommended for that disease are to be employed.

## EMPHYSEMA OF THE LUNGS.

In the consideration of pulmonary emphysema at least five types, so called, of the affection are to be noted, namely: (1) Hypertrophic substantive, idiopathic, or large-lunged emphysema; (2) senile or small-lunged emphysema or senile atrophy of the lungs; (3) compensatory or vicarious emphysema; (4) acute vesicular emphysema; (5) interstitial or interlobular emphysema. Although all but the last named of these affect the vesicles, the first only is a distinct pathological and clinical entity for which the term emphysema is entirely appropriate. This type is very clearly differentiated from the others and to it reference is always made when the unqualified term emphysema is employed. For these reasons it seems wise first to consider the etiology and pathology of this form and later briefly to state the chief characters of the other varieties.

1. **Substantive or Large-lunged Emphysema.—Etiology.**—Very many factors have been assigned as the chief or contributing cause of this disease. Two points appear definitely established, namely, that emphysema occurs rarely or never in lungs that are not congenitally weak, and, second, that the actual exciting cause is increased intravesicular tension. So far as the first factor is concerned the disease is hereditary in that the predisposition is transmitted in the shape of pulmonary tissue that is unable successfully to withstand heightened intra-alveolár pressure. This view receives strong support from the number of family series of cases reported and also from the not infrequent development of the disease in childhood. The condition in the parents most often underlying this tendency is emphysema itself, but gout appears worthy of mention. The fundamental nature of the inherited weakness has not been clearly determined. A defect in the elastica of the lung is the most reasonable supposition, and although this has not been proven and possibly is incapable of satisfactory demonstration, it nevertheless best explains the changes that occur. Heightened intravesicular pressure may be brought about by forced inspiratory or expiratory action. The literature dealing with the relative importance of these two factors is voluminous. The first was the view of Laennec and in a modified form has been upheld by Gairdner. As will be mentioned later this factor is undoubtedly active in the production of compensatory emphysema, but that it is of considerable importance in the type under consideration is to be regarded as doubtful. When lobules or parts of lobules are eliminated from the air-containing capacity of the lung by varied processes, particularly in the nature of inflammation of the smaller bronchioles, the neighboring vesicles become at least temporarily overdistended. This is admitted by all, and if the plugged areas remain permanent, typical compensatory emphysema results. To induce a universal distribution of the lesion, the obstruction must shift, and thus in succession

bring all parts of the lung under the increased strain. If this repeatedly occurs the elasticity of the vesicular walls finally becomes permanently lessened and an overdistended condition of the vesicles is the result. From the very nature of this process it does not appear that it can be held accountable for the production of the great majority of the cases of large-lunged emphysema.

The expiratory factor in the production of increased intravesicular tension and consequently of emphysema must now be regarded as a more satisfactory explanation. It is brought about by increased pressure upon the lung by the chest wall at the time when free egress of air from the organ is prevented by abnormal conditions in the respiratory passages, particularly the narrowing of the glottis that occurs during coughing. By inducing the violent expulsive efforts made during this act, chronic bronchitis is one of the most fruitful causes of emphysema. Whooping-cough is also a cause. During these efforts the sternum and costal cartilages are pushed forward, the ribs become less oblique, the outer and posterior parts of the lungs are subjected to increased pressure, and the spaces in which lie the apices and anterior margins of the organs are made more capacious, thus permitting overdistention of the vesicles in those areas. Confirmative of this explanation is the fact that in these locations emphysema first appears and later becomes most conspicuous. The increased tension produced in the lungs of glass-blowers and the players of wind instruments, as well as that induced by heavy lifting also tends to produce emphysema. That they are so important as at one time believed, however, is not borne out by recent clinical and anatomical studies, it being shown that with care a wind instrument can be blown without injuring the lungs of the player. It may be said in conclusion that doubtless in some cases both inspiratory and expiratory distention are active in the production of emphysema, the former especially in those parts of the lung subjected to greatest pressure by the thoracic wall. In chronic bronchitis there is not infrequently the foundation for both series of phenomena.

In the etiology of the disease then must be included those conditions which tend to produce bronchial or other changes that in turn cause increased expiratory effort. Among these should be mentioned the inhalation of the various types of dust. Of actual predisposing diseases, bronchitis and asthma are the most important. Regarding age, substantive emphysema more frequently develops in early and middle adult life. That in old persons is commonly of the type of senile atrophy of the lung. Rapidly developed emphysema, as would be inferred from what has been said regarding hereditary weakness of the lung, is more apt to occur in children, but, as pointed out by Hoffmann, these subjects in many instances make a partial or complete recovery instead of passing on into the chronic form of the affection. As to sex it is probable that women are less often affected only because they are less exposed to what may be designated exciting causes of the disease.

**Morbid Anatomy.**—The emphysematous lung is excessively large and does not collapse when the chest wall is opened. The anterior margins of the two organs may meet or even overlap, these portions, together with the apices and to a lesser extent the basal margins, being particularly affected. The increased space they occupy is obtained by the displacement forward of the sternum, the more horizontal position of the ribs, and the crowding

of the heart to the unaffected side if the lesion be unilateral or downward if bilateral; the diaphragm is also depressed. The costal cartilages are often calcified. The pleura over the emphysematous areas is dry and pale and often contains no pigment; when the pigment is absent in areas only the condition is known, after Virchow, as pulmonary albinism. The affected areas, although not commonly œdematous, pit on pressure, a proof of the loss of elasticity. Congestion is not usually present, and, unless it is, the lung is decidedly paler than normal. The organ is below the average weight and to the palpating finger has a peculiar spongy feel well described by Laennec as that of a pillow of down. Crepitation is lacking in the most emphysematous areas. Along the margins may be found prominent bullæ varying in diameter from 0.5 to 2 cm. These are formed by the coalescence of distended vesicles and in contradistinction to the somewhat similar appearing blebs found in interstitial emphysema cannot be made to change their location. When the organ is incised many of these bullæ do not collapse, but remain as distinctly outlined spaces; they show especially well in specimens that have been inflated and then dried before incision. At autopsy the increased size of the individual vesicles exposed on the incised surfaces is apparent to the naked eye. The smaller bronchi may also show dilatation.

**Morbid Histology.**—Microscopically two lesions are conspicuous. The first is atrophy of the vesicular septa which show varied degrees of thinning. Many of them largely disappear, leaving only short ends projecting into the space formed by the coalescence of the alveoli which originally were divided by the septum. In this way the union of a large number of vesicles produce the bullæ previously mentioned. The loss in septal tissue means also a diminution of the vascular field of the lung and consequent imperfect aëration of the blood, this in part explaining the dyspnœa which is of one of the prominent symptoms of the disease. The second lesion of importance consists of changes in the elastic tissue. The fibers of this substance lose their normal wavy outline, become swollen, and often undergo fragmentation. In marked degrees of the change, elastica as such entirely disappears, only a few granular fragments marking the site of the former fibrils. The bronchi are commonly inflamed and usually show thickening of the walls; the smaller tubes may be dilated. Pigmentary infiltration is commonly slight.

**Associated Lesions.**—These are hypertrophy or dilatation of the right heart or possibly of the entire organ; atheromatous changes in the pulmonary artery with, in some instances, dilatation of that vessel; changes including pigmentation, atrophy, and fibrosis in the liver, spleen, and kidney depending upon congestion secondary to the obstructive lesion in the lung.

2. **Senile or Small-lunged Emphysema.**—This is a disease affecting old persons, and, although it possesses some of the histological features of emphysema, would more correctly be grouped among the atrophies as senile atrophy of the lung. The chest presents a condition entirely different from that in the type just described. It is small, the ribs are more oblique than usual, and the attached muscles are wasted. The lung is decidedly smaller than the normal organ; it collapses when exposed and not infrequently contains accompanying lesions, as congestion, œdema, or even infarction. As in the preceding type, the intervesicular septa are atrophied and broken and the resulting coalescence of numbers of alveoli give rise to large spaces with remnants of vesicular walls showing

on the inner surface. These large bullæ may be so numerous and extensive as to compose the lung almost entirely. The bronchi are often dilated. The septal atrophy here appears primary, the resulting large vesicles being thus produced without the intervention of heightened air pressure.

3. **Compensatory Emphysema.**—Compensatory emphysema is the form that develops in portions of the lung when other parts are airless and is quite satisfactorily accounted for by the inspiratory theory. It may be temporary in point of duration, as when developing in the unaffected lobules in cases of bronchopneumonia. In such instances it is really a physiological overdistention with stretching of the alveolar walls, which on withdrawal of the cause assume their normal condition. More often, however, it is lasting, the vesicular walls undergoing the atrophic changes already described. The latter type is seen in the lung in cases of new-growth, especially of multiple metastatic nodules, between and around tuberculous areas or isolated fibroid patches, and particularly in chronic interstitial pneumonia. In the presence of pleural adhesions the condition also develops.

4. **Acute Vesicular Emphysema.**—This condition clearly should not be placed in the group where long-continued usage still keeps it. It is a functional overdistention of the air vesicles coming on rapidly in cases of acute bronchitis or asphyxia or at times during attacks of angina pectoris or of asthma. Relief from the condition or death ensues before the vesicular walls atrophy and consequently the affection is not truly emphysema.

5. **Interstitial Emphysema.**—Interstitial emphysema is characterized by the presence of air in the connective tissue of the lung and is due usually to the rupture of air vesicles during violent expiratory efforts in coughing, as in whooping-cough and paroxysms of like severity. The distended vesicles in vesicular emphysema may give way and thus allow the air to reach the abnormal location. The condition is also caused by wounds of the lung from without, as by fractured ribs or other penetrating objects. As pneumothorax may arise from pleural infection by gas-producing bacteria it is possible that their presence in the connective tissue of the lung might cause an interstitial emphysema. This type is readily diagnosed postmortem by the presence beneath the pleura of variously sized blebs, sometimes 2 cm. or more in diameter, which by pressure can be made to change their place, thus differing from the stationary bullæ in vesicular emphysema. Rupture of these blebs may produce spontaneous pneumothorax, and in addition, when occurring near the root of the lung, air occasionally passes into the mediastinum and even the structures of the neck, giving rise to emphysema of those tissues.

**Symptoms.**—As the evolution of the disease is slow, its symptoms do not manifest themselves abruptly but are of gradual onset and progressive development. It is not unusual for patients to suffer ill health a long time before distinct evidence of emphysema can be elicited.

One of the chief symptoms is dyspnœa. In the beginning of the disease, before pulmonary distention has become far advanced, it may amount to no more than slight shortness of breath upon exertion, but as the lungs lose more and more of their elasticity and the capillaries in the alveoli become obliterated, it grows constantly worse. In a person suffering from advanced emphysema, inspiration is short and quick, while expiration is much pro-

longed. This peculiarity in breathing is due to loss of elasticity in the lung, upon which, as is well known, expiration largely depends. When this attribute is lost the air is not expelled from the lungs in a normal manner, all the auxiliary forces of expiration being summoned into play. Even then the result is not complete and a certain excess of residual air remains. When the dyspnœa becomes unusually severe, especially during a paroxysm of asthma or when an exacerbation of bronchitis occurs, the patient will often be found pressing forcibly upon his sides in an endeavor to drive more air out of his lungs. The most characteristic circumstance about the dyspnœa therefore is that it occurs with expiration. The respirations are not much increased in frequency, the principal change being in their rhythm.

A considerable influence is exerted upon the intensity of the dyspnœa by the degree of severity of the associated bronchitis; thus when exacerbations of the latter occur and the secretion in the tubes becomes more copious, the difficulty of respiration will be augmented, whereas, on the other hand, during periods of comparative freedom from cough and bronchial catarrh only slight dyspnœa is experienced. There is nothing peculiar about the cough. As it is more or less constant, it not only harasses the patient, but saps his strength as well, and moreover hastens the development of cardiac complications. The sputum is that of ordinary chronic bronchial catarrh except in those cases in which asthma is present, when it may contain Charcot-Leyden crystals and Curschmann's spirals.

The heart suffers as well as the lungs, and symptoms of circulatory disturbance are characteristic of the later stages of the disease. The weakness of respiration, the mechanical effect of the retained air upon the lungs, the paroxysms of coughing, all serve to make aëration of the lungs defective and consequently diminish oxygenation of the blood. This condition is at first shown by blueness of the lips and slight lividity. Upon severe exertion the lividity may become so augmented as to constitute distinct cyanosis, and it is likewise increased when exacerbations of the bronchitis occur.

As more and more bloodvessels in the lungs become obliterated, and as an increasing number of alveoli become distended, the work of the right side of the heart is progressively increased. It undergoes hypertrophy in an endeavor to overcome the resistance with which it has to contend, but sooner or later compensation fails because the destructive process in the lungs is unlimited in its potentiality of development, whereas the heart can only hypertrophy to a certain extent; moreover, the functional disturbances engendered by the pulmonary lesions are so violent as to vanquish the saving effort put forth by the increased cardiac action. Thus it is that compensation fails and the heart dilates. Under these circumstances the dyspnœa and cough become more distressing and the cyanosis more pronounced. Digestive and intestinal disturbances ensue. The liver becomes congested, the extremities swell, and dropsy sometimes occurs. That the result of such profound changes is a serious impairment of the general health scarcely need be stated. Nutrition suffers and the patient grows weak and emaciated. Hæmoptysis and hæmatemesis sometimes take place; epistaxis, too, is not uncommon when there is much venous congestion. Hemorrhoids also are frequently associated with emphysema, being due to hepatic congestion.

**Physical Signs.**—The thorax of a person suffering from emphysema presents marked abnormalities, the anteroposterior diameter being much

increased, so that it may equal or even exceed the lateral diameter. It is only in exceptional cases, however, that a tracing obtained with the cyrtometer will show equality of the two diameters. The shoulders are rounded, the curve of the spine increased, the clavicles prominent, and the subclavicular spaces obliterated; the sternum and ribs bulge out anteriorly and the intercostal spaces are widened. These changes give the chest a barrel shape, and make the neck look unusually short. Owing to the cardiac disturbances the superficial veins become dilated and stand out prominently on the skin. They show very plainly in the neck, distention sometimes occurring rhythmically with each expiration, so that they have the appearance of pulsating tumors. A chain of dilated venules is often seen on either side of the sternum, running around the costal arch at a level corresponding to the attachment of the diaphragm. Pulsation in the epigastrium is also frequently noticed.

Instead of expanding with the act of inspiration the chest becomes elevated and its lower part may even retract when an inspiration is taken.

Palpation will sometimes show that vocal fremitus is diminished, although it frequently happens that no abnormality in this respect is demonstrable. Rarely the apex beat of the heart may be felt in the epigastrium.

The percussion note is increased in resonance, or may even be distinctly tympanitic. The pulmonary area is always increased, often extending posteriorly to the lower costal margin and reaching anteriorly to the level of the sixth or perhaps the seventh rib. The area of cardiac dulness is greatly diminished and may be entirely obliterated. Even when the heart is enormously hypertrophied it may happen that only a small area of cardiac dulness can be detected owing to the fact that the distended lungs almost entirely cover it.

The diaphragm is at a lower level than it is in health and it moves the liver and spleen, and the stomach as well, down with it. Liver dulness often begins in the seventh costal interspace. The area of splenic dulness cannot, as a rule, be well defined owing to the distention of the lung on the corresponding side. The stomach is often dilated, but it cannot always be outlined for the same reason that it is not always possible to make out the boundaries of the spleen.

Upon auscultation the breath sounds are found to be weak. The inspiratory sound is short and labored, the expiratory sound prolonged and feeble. As bronchitis is frequent, rales and rhonchi are often heard in all parts of the chest. A peculiar crepitant sound which has been attributed to friction of the distended portion of the lungs upon the pleura is also sometimes present.

The cardiac sounds are feeble owing to the margins of the distended lungs overlapping and covering more or less of the heart. As cardiac involvement becomes more pronounced, the signs of tricuspid insufficiency manifest themselves, a systolic murmur being heard over the ensiform cartilage or at the right of the sternum at about the fifth interspace.

**Complications.**—The distinct complications of emphysema are pneumothorax and interstitial emphysema. The former results from the rupture of pulmonary vesicles, the latter sometimes follows a violent paroxysm of cough or overexertion.

**Diagnosis.**—The general appearance of a person suffering with advanced emphysema, together with the symptoms complained of and the signs elicited upon examination of the thorax, usually suffice to prevent the disease from

being confounded with other affections. The characteristic dyspnœa, the cyanosis, and the shape of the thorax make a picture which is not formed by any other disease. There is, however, a disease which presents some symptoms and signs common to emphysema, namely, pneumothorax, but its onset is sudden instead of gradual, it is limited to one side of the thorax, and the deformity which stamps emphysema is not present. Further, in emphysema the intercostal spaces are not obliterated as they are in pneumothorax.

Fränkel states that extensive adhesions of the parietal pleura to the lungs may give rise to symptoms closely resembling those of emphysema and cause hypertrophy and dilatation of the right side of the heart. When the entire surface of the pleura is not adherent, the relatively free portions of the lung may become distended. If it happens that only the lower portions are adherent, the upper part of the lungs may become distended and produce alterations in the conformation of the upper part of the thorax. This condition, however, must be exceedingly rare. It would be differentiated from emphysema by the absence of the physical signs relating to the lower part of the pulmonary area. If of long duration, however, the process would amount to the same thing as a moderate degree of emphysema.

The symptoms produced by the pressure of tumors upon the trachea and larger bronchi ought not to be mistaken for emphysema, for although dyspnœa is present and the vesicular murmur diminished there is no deformity of the thorax.

**Prognosis.**—Emphysema is incurable, but much can be done to render the patient comfortable and to prolong his life. Even when left to pursue its course unhampered it is not a rapidly fatal disease; so that persons affected with it often live for years, although their existence is always shortened.

Seasonal changes exert a material influence upon the comfort of emphysematous patients and likewise upon the severity of their disease. In winter the bronchitis is more subject to exacerbations than it is in summer, and for this reason patients are often worse during cold weather than at other times of the year. The danger is, of course, increased by these exacerbations.

As long as cardiac compensation is maintained there is no immediate danger of death unless some complication sets in, such as bronchopneumonia and influenza. Dropsy and pulmonary hemorrhage are very serious complications.

**Treatment.**—As emphysema is an incurable malady the efforts of the physician should be particularly directed to preventing its development in those who are predisposed by reason of chronic bronchitis and asthma, and also to delaying, as far as it is in his power, the evolution of the disease when it is detected in its incipient stage. A careful regimen will greatly reduce the liability of the development of emphysema and also materially prolong the days of those who are subject to it.

Persons affected with chronic bronchitis or asthma should take the utmost pains to avoid exposure to cold and dampness, and should be constantly on their guard against sudden changes of temperature. Those whose means permit it should spend the colder months of the year in a warm, sheltered climate at a moderate elevation, such as that of Egypt and the Riviera, or Southern California. If the cough is very dry and expectoration scanty, moist climates are suitable. In summer, residence in localities situated

near pine forests is desirable. The altitude must be moderate and not high, and a place should be selected where strong winds do not prevail. The Maine woods and the Adirondack Mountains are suitable places for summer residence. In Europe the health resorts of the Black Forest and the Fichtelgebirge in Germany may be tried. During bad weather these persons should not venture out-of-doors. They should be warmly clad at all times. Occupations demanding great physical exertion should be relinquished, as should also those in whom there is exposure to dust or irritating fumes.

The diet should be substantial, but composed of food that is easily digested. The bowels must be regulated, laxatives being used if necessary. These rules of hygiene also apply to those who are already affected with the disease.

Different mechanical appliances have been employed for the purpose of facilitating the expulsion of air from the lungs. Thus, an elastic belt has been worn around the lower part of the thorax, and Strümpell's apparatus consisting of two boards joined at one end by an elastic band, has been used, one board being placed on each side of the thorax and pressure made during expiration by the patient grasping the anterior ends and bringing them forcibly against the body. A more elaborate apparatus devised by Steinhoff has also been used for the same purpose. Swedish movements, consisting of direct pressure upon the ribs or forcible rotation of the trunk upon its axis alternately from one side to the other, have been employed for the purpose of immobilizing the ribs, and thus arresting the changes in the configuration of the thorax.

Hydrotherapeutic measures are valuable adjuncts, as they exert a favorable effect upon the heart and circulation. Hot and cold douches, the cold rub, and the cold half-pack have all been used with benefit. They should not be employed as a matter of routine, but should be selected for individual cases as the physician may deem advisable. The hot douche has been used with good result in connection with some of the pneumotherapeutic measures which we shall consider next. It is thrown upon the thorax with the idea that its stimulating effect will aid the expulsion of air from the lungs.

Various methods of pneumotherapy have been used, and it has been asserted that brilliant results have followed their employment. The condensed-air bath was highly recommended by Dujardin-Beaumetz, but it is doubtful if any good results follow its use other than those which depend upon its stimulating effects upon the bronchi. The distention of the lungs, of course, cannot be influenced by it. For the subjects of advanced cardiac disease and arteriosclerosis it would be dangerous.

Expiration into rarefied air has been tried, both alone and in conjunction with the condensed-air bath. It causes retraction of the thorax, and increases the force of expiration, thus causing more air to be expelled. This method seems rational and, indeed, some of its strongest partisans have asserted that most brilliant results have been secured by its employment. Waldenburg, especially, was an ardent advocate of its merits. That many of the assertions relative to its value were extravagant has been proven by further clinical experience and scientific investigation. We are much indebted to Schreiber, of Königsberg, for a thorough investigation of the effect of the procedure. There is no doubt that temporary relief is afforded in some cases by the inspiration of rarefied air, but in others no benefit is derived. Perhaps some of the improvement which was supposed to have resulted from the method was due to the mental effect produced.

The inhalation of mineral waters by atomization and vaporization also requires mention. Sulphur and arsenical waters have been extensively used in France for this purpose, and it is stated that relief has often followed their employment. They are inhaled in the form of a fine spray, and are also vaporized. It is not to be doubted that they frequently relieve the symptoms of bronchitis. At Luchon, in France, the inhalation of sulphuretted vapors by the method known as "humage," has been practised, and is said to afford good results. It is not improbable that the regimen of living followed at these resorts, together with the baths and internal use of mineral waters, contribute to bring about a large part of the relief.

Venesection is valuable for the relief of severe dyspnœa and cyanosis. The extraction of a pint or a pint and a half of blood will sometimes save a patient who is gasping for breath, and so cyanosed that he is black in the face. Venesection should not be used in any but the most severe cases.

From what has already been said concerning the morbid anatomy of emphysema it is evident that the treatment of the disease by drugs must be directed to combating symptoms as they arise. Bronchitis and asthma must be combated, and circulatory disturbances controlled as much as possible. Exacerbations of the bronchitis are to be treated by the use of expectorants, such as ipecacuanha and small doses of apomorphine, by counterirritants such as turpentine liniment or mustard applied to the chest, and by sedative inhalations such as a mixture composed of equal parts of compound tincture of benzoin and paregoric, of which a tablespoonful is used to the pint of hot water. When there is profuse secretion of mucus in the bronchi, an emetic dose of apomorphine will sometimes cause its expulsion and afford relief. For the constantly associated chronic bronchitis ammonium chloride is probably as good a drug as we possess. It may be given in 5-grain doses every four hours, and if the cough is very distressing, gr. $\frac{1}{6}$ (0.01 gm.) of codeine sulphate or gr. $\frac{1}{12}$ (0.005 gm.) of heroine may be added. This drug may be administered in fluidextract of licorice or syrup of wild cherry. Terpin hydrate and creosote may sometimes be used with advantage. The thing to be feared about all these expectorants is that they may disorder the stomach. If they do they must be stopped at once.

Laxatives are often required to overcome constipation and relieve flatulence.

For an attack of asthma a hypodermic injection of gr. $\frac{1}{4}$ (0.016 gm.) of morphine and gr. $\frac{1}{100}$ (0.0006 gm.) of atropine may be administerd, and if the condition of the heart does not contra-indicate it, a few whiffs of amyl nitrite may also be given.

For failing cardiac action, digitalis in small doses and strychnine fulfil all indications. 5 drops of tincture of digitalis three times a day will support a failing heart and prolong the patient's comfort for a considerable period. Large doses of strychnine, for instance, gr. $\frac{1}{20}$ (0.003 gm.) three or four times a day, for a short time, not only stimulate the heart, but also exert a similar effect upon the respiratory centre. It is not at all uncommon for marked improvement in the bronchitis to take place under the use of these drugs.

When dilatation of the heart has occurred and venous congestion is marked, larger doses of digitalis are indicated. 10 or 15 minims may be given every four hours, but, of course, the cumulative action of the drug must be borne in mind, and a watch kept for its manifestations. Digitalis is often

less efficient in the cardiac disease of emphysema than it is in other forms of heart disease, for the reason that it does not materially influence, and certainly cannot arrest, the lesions in the lungs upon which the heart trouble depends.

The iodides have long been employed in the treatment of emphysema. At one time it was thought that they might prevent destruction of the pulmonary vesicles, but such a theory is not tenable. The good which follows their administration depends upon the effect they exert upon the concomitant bronchitis and upon their action on the bloodvessels. They lower arterial tension and may retard the development of arteriosclerosis. 5 grains (0.3 gm.) of the iodide of sodium or ammonium may be given in water or milk after meals. The syrup of hydriodic acid may be substituted when the ordinary iodides disagree with the stomach.

## GANGRENE OF THE LUNG.

**Etiology.**—Gangrene of the lung is due to partial or entire necrosis of a portion of the organ and added infection which probably always is mixed in character. Necrosis alone, without the phenomena of gangrene and infection by certain of the bacteria which are often found in gangrenous tissue, does not ordinarily give rise to this process. Studies indicate that saprophytic putrefactive bacteria are a necessary adjunct to the already necrotic and usually previously infected tissue, but no special bacterium which in every case acts as the exciting cause has been isolated. As a consequence, gangrene is found in connection with processes that lower the vitality of pulmonary tissue by interfering with the blood supply and which favor, or actually carry with them, infection of the necessary type. Just why gangrene occurs in certain instances and not in others under what appear to be similar circumstances in both is not perfectly clear. Undemonstrable difference in tissue resistance is the most reasonable explanation.

Among the important causes of gangrene are: (1) Lobar pneumonia. This disease does not often terminate in this manner, Aufrecht meeting with no instance in 1500 cases. It may or may not be preceded by abscess formation. (2) Aspiration pneumonia. In these cases the causative agents are drawn into the finer bronchi where the process begins. (3) Pulmonary embolism. This is most frequently a cause when the emboli are from a septic focus, but the plugging of a large vessel by a non-infected embolus may induce the condition. Infectious thrombosis of the cerebral sinuses is in this way an important cause, abscess of the lung not uncommonly being first induced. Any of the causes mentioned in the consideration of pulmonary infarction, especially if the primary focus be infected, may result in gangrene of the lung. (4) Foreign bodies in the bronchi or bronchiectatic cavities may lead to gangrene. In either case intensely infectious material gathers in the affected area and is propagated into the surrounding tissue. Tuberculous cavities may also act in this manner. (5) Trauma. This may exert its effect in the way of simple contusion of the chest wall or by actual perforation of the wall and direct injury and infection of the lung. (6) Infectious and debilitating diseases, as typhoid fever, diabetes mellitus, and long-continued bronchopneumonia. (7) Suppuration in the lung. (8) Pressure upon the pulmonary vessels by aneurism or new-growths in the

lung or in adjacent structures. Gangrene is prone to follow rupture into the lung of cancer originating in contiguous tissues.

**Morbid Anatomy.**—Gangrene of the lung may be diffuse or circumscribed. The former rarely occurs, but may terminate an attack of croupous pneumonia, affecting, as does that disease, an entire lobe or even a whole lung. Occlusion of a large branch of the pulmonary artery may also induce this type. It corresponds to the so-called spreading gangrene of the extremities in that the gangrenous area possesses no definite line of separation from the surrounding structure, the grayish or dark necrotic area passing gradually into the inflammatory zone of recognizable pulmonary tissue that surrounds it.

Circumscribed gangrene may be in the form of single or multiple foci, but in either instance the diseased tissue is sharply separated from the surrounding lung. The affected area is at first brown or slightly reddish in color, but soon becomes dark and finally almost black, liberated pigment from disintegrating blood cells being largely responsible for the coloration. A greenish tinge may appear, but this is usually not so prominent as in the gangrene of external parts. Softening and disintegration soon occur and a cavity is produced. Unless of large size the cavity is not always entirely empty, but contains one or several irregular masses of softened and discolored lung tissue which have not entirely liquefied. In the ragged wall or even passing through the cavity may often be found bloodvessels and bronchi which have resisted the necrotic processes. When cavities are formed, the characteristic sputum appears and the odor of pulmonary gangrene; hemorrhage may occur, the vessels in the affected part not usually being firmly thrombosed. Surrounding the inner wall of the cavity is a zone of congested or hyperæmic tissue and external to this an œdematous area. Leukocytes appear in the outer zones, and if the gangrenous focus be small and the reparative powers of the living tissue active, connective-tissue formation with healing of the necrotic area may limit the process and lead to recovery of the patient. This unfortunately is not a common occurrence.

**Symptoms.**—As in the case of pulmonary abscess, so, too, in gangrene, the manner of onset and the symptoms of the disease depend somewhat upon the causes which give rise to its development. Thus when it develops in the course of specific affections, the symptoms of the latter may predominate at first, although pulmonary disturbances may even then be present in lesser degree, for the reason that it is not uncommon for the gangrenous process to be preceded by lobular pneumonia, and moreover because some infiltration is invariably produced in the lung before distinct necrosis takes place. When due to croupous pneumonia, its onset is usually marked by a chill and elevation of temperature some days after crisis has occurred. When cavities in the lung become necrotic the process is usually slow and marked by gradual increase in the severity of the symptoms previously present.

It will be seen, then, that, as a rule, symptoms referable to the respiratory organs, together with some elevation of temperature, loss of appetite, and weakness precede the more characteristic manifestations of gangrene, and that they may continue for days or weeks before the latter become pronounced.

Although the onset is not sudden in the sense that the disease attacks persons who were previously in good health, the establishment of the gangrenous process is, however, usually announced by a marked exacerbation

of the prodromal symptoms, which is often very abrupt. The temperature rises higher and chills may occur, the cough becomes worse and dyspnœa sometimes ensues. As soon as the necrotic area communicates with a bronchus the sputum undergoes a change. While up to this time it may have possessed the characteristics of pneumonic sputum, contained a little blood, or merely have been such as is expectorated in bronchitis, according to the individual case, it now is found to possess an attribute peculiarly its own. This property is an extremely fœtid odor such as is not met with in any other disease, and which has been variously described as resembling that of fæcal matter, dung-water, or putrefying flesh. This odor is transmitted to the patient's breath, and is so intense and penetrating that it is often diffused through the air of the entire room in which the patient is confined.

With the supervention of this sign the subjective symptoms become accentuated. Fever increases, the temperature rising perhaps as high as 104° or higher; the pulse becomes rapid, soft, and compressible; the cough more distressing, and exhaustion greater; any attempt to move increases the severity of the symptoms. The face is pale and drawn, the tongue dry and cracked, the extremities cold, and the whole body sometimes covered with a cold sweat. Anorexia is complete and vomiting may occur, both being due no doubt to the foulness of the expectoration. Diarrhœa may also be present. It has been observed that the patient is inclined to lie on the affected side, thereby causing gravitation of the secretion and lessening the frequency of expectoration. Naturally the expulsion of a considerable quantity of this foul sputum during a paroxysm of cough should be less offensive than constant spitting of smaller quantities.

The expectoration is usually abundant. When the sputum is first coughed up it is of a dirty gray or brownish color. If it be collected in a glass it will be found to separate into three layers: In the bottom of the glass there is a thick, opaque stratum, of a yellow or greenish-brown tinge, consisting of pus, fragments of lung tissue, and gray or yellow, grumous masses. Above this stratum is a transparent layer of serous fluid, perhaps having a few flocculi floating in it, while superimposed upon this is a thick, opaque, frothy layer, of a dirty yellow color. Microscopic examination of the lowest stratum reveals the presence of leukocytes, red cells, epithelium, and elastic tissue. Traube has called attention to the fact that elastic tissue may be absent, and its absence is attributed by Filehne to the action of a bacterial ferment which he discovered, and which is similar to trypsin. The clot-like plugs are found to contain fatty acids.

A special form of pulmonary gangrene which requires mention is that which occurs in diabetes mellitus. Its course is very chronic, lasting perhaps for many months. It usually begins as a pneumonic process with profuse expectoration of blood-stained sputum, which finally becomes malodorous, although it is never so offensive as that in other forms of the disease. Hemorrhages are of frequent occurrence.

**Physical Signs.**—In the beginning of the disease examination of the thorax fails to reveal distinctive signs. There may be areas in which the percussion note is somewhat impaired, and upon auscultation moist rales and diminution of the breath sounds may be heard. As the morbid process advances and the pneumonic infiltration around it becomes more extensive, dulness may become more pronounced. This is more likely to be the case

when the gangrenous area is superficial than when it is deep. As softening of the dead area takes place and the necrosed tissue begins to be expelled, the signs of cavity formation may appear. The rales become larger and more moist and amphoric breathing and pectoriloquy may be heard. Owing to the accumulation of secretion in the tissue around the cavity, subcrepitant rales may be heard in an area beyond its borders. Bronchial breathing may be present, as in some cases extensive consolidation exists around the cavity.

**Complications.**—The principal complications are hemorrhage, empyema, and metastatic abscesses. Hemorrhage is prone to occur; it is due to involvement of bloodvessels in the gangrenous process. When the latter is situated superficially it may extend to the pleura and cause a portion of the latter structure to slough away, with the result that pyopneumothorax is produced. The pleura may also become inflamed without being ruptured, and the effusion which is poured out is generally purulent.

Metastatic cases owe their origin to septic emboli resulting from disintegration of blood clots which form in the vessels of the lung. They are commonly located in the brain, although they may occur in the liver, spleen, and kidneys. Their presence in the brain gives rise to symptoms of cortical irritation, to hemiplegia, and to monoplegia.

**Diagnosis.**—The diagnosis of pulmonary gangrene rests upon the putrid odor of the breath and sputum and the physical characteristics of the latter. The physical signs of cavity alone are of no worth, because they may be produced by other lesions, but when taken in conjunction with the diagnostic points just mentioned they are of corroborative value. The previous condition of the patient and the mode of onset and evolution of his present trouble must be taken into account, especially in those cases where the process is not acute. The degree of prostration will also serve as an index.

In putrid bronchitis the odor of the breath and sputum is not so foul as it is in gangrene, and, moreover, elastic tissue is never expectorated; the constitutional disturbances also are not so severe. It may be very difficult to distinguish between cases of ulcerating tuberculous cavities and gangrene, although the tubercle bacillus may be found in the sputum of the former disease. Tuberculous cavities may, however, become gangrenous, and in this case the bacterial findings are of little value.

**Prognosis.**—Gangrene of the lungs is a very fatal malady. In the acute form death usually occurs within a few days after the development of the disease. It may result from hemorrhage, acute toxæmia, or complications such as pneumothorax or metastatic abscesses. In the subacute and chronic cases the patient may die from exhaustion or sepsis. When the lesion is small and circumscribed recovery may take place.

**Treatment.**—Little can be expected from medical treatment. The patient's strength should be maintained, if possible, by the use of highly concentrated liquid food, given in small quantities at frequent intervals, with the liberal administration of alcohol. Large doses of quinine and tincture of chloride of iron may be given in the hope that they will combat sepsis, but if the iron disturbs the stomach it must be discontinued.

Inhalations of turpentine, creosote, and carbolic acid have been recommended. They may lessen somewhat the terrible stench created by the decomposition going on in the lung, and perhaps soothe the irritated bronchi, but they cannot arrest the gangrenous process. For cough and

pain morphine may be given, and it may likewise be administered when hemorrhage occurs.

For subacute or chronic gangrene such as occurs in diabetes or chronic tuberculosis, supportive treatment is indicated, together with the use of stimulating inhalations, such as turpentine or oil of sandalwood. As to surgical treatment, it may be stated, as a rule, that operation is indicated early in every case in which a single limited lesion can be isolated, and the patient's condition is grave. If no alarming symptoms are present a little delay may be tolerated, but in any event the removal of a gangrenous focus would seem to be rational. If the lesion cannot be located, as will happen to the majority of cases, unless pulmonary destruction is extensive, exploratory incision may be made in an attempt to find the sphacelated mass. Empyema demands immediate operation. When small multiple foci are present operation, of course, will be of no avail.

## ABSCESS OF THE LUNG.

**Etiology.**—Abscess of the lung is a term often applied indiscriminately to suppurative conditions of whatever type developing in that organ, although in many of them the lesion does not possess the characters of abscess in other viscera. This is due largely to the anatomical peculiarities of the lung and, although it gives rise to some discrepancy between clinical and pathological descriptions, practically the point is not one of extreme importance. Primary suppuration in the lung almost never occurs and consequently, although pus is found in the organ under varied circumstances, pulmonary abscess, properly so called, develops only in two groups of cases: (1) In areas of previously diseased lung tissue, and (2) as the result of the lodgement of infected emboli. In the former group are a number of conditions. Croupous pneumonia is occasionally followed by suppuration, the resulting abscess being either single and possibly occupying a large part of a lobe, or more often there are multiple smaller foci through the pneumonic area. This type is to be differentiated from a condition arising in pneumonia and commonly known as purulent infiltration, in which during resolution an excess of liquefied exudate macroscopically resembling pus, bathes the pulmonary tissue and gives rise to the name; microscopically and bacteriologically this material in such cases is shown not to be pus. In the nature of trauma with added infection, aspiration and deglutition pneumonias frequently produce suppuration by carrying pyogenic bacteria into the lung with food or other substances. The former is apt to occur after operations upon the mouth, tongue, or throat, or as a sequence of suppurative lesions of the upper respiratory passages. Foreign bodies in the bronchi or lungs may be the cause of suppuration. Puncture of the pleura by an exploring needle or by a fragment of a broken rib or other body may be followed by pulmonary abscess. Emboli from whatever source, bearing pyogenic organisms and lodging in the lung, give rise to the so-called metastatic abscesses. These are usually small, nearly always multiple, and often extend to the pleura as cone-shaped areas, although abscesses may arise without the formation of definite infarcts. If the abscess be superficial, pleurisy develops over it and rupture into the pleural sac is not uncommon, the latter giving rise to empyema or possibly pyopneumothorax.

Other instances of suppuration in the lung, at times designated as pulmonary abscess, are those in which the organ is invaded by pus from contiguous structures. This may occur in localized empyema, from extension into the lung of cancer of neighboring tissues, in suppurative lesions of the mediastinum, and in cases of pus formation in the abdominal cavity, particularly hepatic abscess and suppurating echinococcus cyst of the liver, which reach the lung through the diaphragm. In most of these cases the pus passes through the lung, gains access to a bronchus, and is expectorated instead of increasing locally by peripheral extension of the necrotic process and thus forming a true abscess. Extension by the lymphatics in these cases may, however, give rise to new foci of pus formation. Another form of pulmonary suppuration in the shape of a diffuse suppurative lymphangitis, peribronchial in location, is sometimes found postmortem, but is unrecognizable during life. In this the pus, which is found in the interstitial structure and larger lymphatic tracts, may be due to infection of the lymphatics by bacteria from the pleura or from the tissues around the root of the lung. Suppuration occurring in a tuberculous cavity as the result of secondary infection is sometimes designated pulmonary abscess.

**Morbid Anatomy.**—As mentioned in discussing the types of the lesion, abscess of the lung may be large or small, the size of a lobe or 2 cm. or less in diameter. The cavity contains the ordinary constituents of pus and usually in addition fragments of lung tissue and the remains of partially disintegrated alveolar epithelial cells. Fragments of lung in the form of alveolar elastica appearing in the sputum form a valuable aid in diagnosis of abscess. The cavity of the acute abscess is bounded by a wall consisting of an inner layer of necrotic lung tissue containing polynuclear leukocytes, a second zone densely infiltrated with inflammatory products, and possibly containing proliferated connective-tissue cells, and a peripheral zone of œdematous pulmonary tissue. In some cases of high-tissue resistance and slow progress of the abscess a limiting wall of new fibrous tissue is formed. If evacuation of the contents is complete, cicatrization of the entire area may take place. Neither of these terminations is common. The wall of a pulmonary abscess may become gangrenous, especially if the pus has been evacuated and the resulting cavity imperfectly drained. If the abscess wall be formed partly by the pleura, as is usual in embolic abscesses, the latter structure will be surmounted by a fibrinous exudate in which pus formation may or may not occur. The result of pleural perforation has been considered under the heading of etiology.

**Symptoms.**—The symptoms of suppuration in the lung vary somewhat in accordance with the cause of the development and the size and number of the lesions present. When due to a septic embolus, the course of septicopyæmia, or one of the more malignant acute infectious fevers, as variola, symptoms of respiratory disturbance may be masked by the general constitutional manifestations of the disease. In other cases, however, cough, dyspnœa, pain in the chest, and the expectoration of purulent sputum will be superadded to the other manifestations, provided that the patient does not early succumb to his general infection.

Abscesses due to the inspiration of foreign bodies are characterized by a septic temperature, cough, dyspnœa, and pain, a syndrome which may be said to characterize all forms of acute pulmonary suppuration; however, in this class of cases, it supervenes shortly after the foreign substance has

lodged in the lung and is not superimposed upon another symptom-complex. It may be that signs of bronchopneumonia have been observed before those of suppuration ensued, although as a rule septic foreign bodies induce pus formation very rapidly.

When suppuration of the lung occurs in lobar pneumonia, its presence will be marked by continuation of the fever beyond the usual duration and failure of the consolidated areas to undergo resolution. The temperature may assume a higher elevation than that at which it was maintained during the course of the disease, but it will usually be characterized by fluctuations, assuming a distinct septic type with morning remissions and evening exacerbations. Dulness will persist over the affected area and bronchial breathing or indistinct breath sounds will be heard upon auscultation. As the morbid process advances and more tissue undergoes liquefaction, and especially after the abscess begins to empty itself, the signs of cavity in the lung may become apparent; amphoric breathing and coarse crepitant rales may then be heard.

The sputum undergoes important changes, becoming grass-green, or sometimes dark brown in color. As soon as the abscess communicates with a bronchus its contents will begin to be freely discharged. Sometimes a gush of pus, so profuse as to fill the patient's mouth and nearly choke him, will suddenly occur. Fragments of elastic tissue are brought up with the expectorated material; they may be large enough to be detected macroscopically, or so small as to require the use of the microscope to reveal their presence. Although disagreeable, the odor of the expectoration is not so foul as in putrid bronchitis and gangrene of the lung.

Not only do these changes in the objective symptoms take place, but alterations in the subjective symptoms may likewise occur. It not uncommonly happens, when a single large abscess has emptied itself in the manner just described, that the fever subsides and the general condition improves, although pus may be discharged for an indefinite period varying from weeks to months; some abnormality of temperature may also persist. The duration of these symptoms will depend upon the rapidity with which the abscess becomes obliterated.

In another class of cases due to pneumonia, defervescence takes place in the regular manner, but in the course of two or three weeks the patient develops irregular fever, cough, and dyspnœa, and after being ill for some time may either begin to expectorate purulent sputum, or be seized with a violent paroxysm of cough and bring up a considerable quantity of pus. Relief may then follow and healing take place, or the abscess fill again, and similar attacks follow. Sometimes the patient enters upon a period of decline, loses weight, runs a hectic fever, and succumbs to the inroads of sepsis.

As was stated in discussing the complications of bronchopneumonia, the minute abscesses which are occasionally formed seldom produce any symptoms. This is likewise the case with those small areas of suppuration which form around new-growths, although they may be responsible for the slight elevations and irregularities of temperature which sometimes occur. These small abscesses are frequently not suspected during life, but are discovered at autopsy. The softening and liquefaction of indurated areas of lung tissue which sometimes occurs in chronic interstitial pneumonia or cirrhosis of the lung, does not give rise to the symptoms above described.

Acute symptoms are not present, nor is the sputum characterized by the admixture of pure pus.

**Complications.**—When a pulmonary abscess is superficial, pleurisy almost invariably results and is very apt to be purulent. The abscess may also break through the pleura and cause empyema in this manner or perhaps give rise to pyopneumothorax. Purulent pericarditis and cerebral abscess are also occasional complications. The suppuration process may also terminate in gangrene. In chronic abscess cavities there is danger of hemorrhage taking place from erosion of vessels in the wall. It is possible, too, that amyloid disease may supervene in chronic cases.

**Diagnosis.**—The diagnosis of abscess of the lung may be very difficult. As already stated, small multiple pyæmic abscesses may not produce distinct symptoms because of the violent disturbance caused by the general infection. When one or more large abscesses communicate with a bronchus so that pus gushes up and fragments of lung tissue are expectorated, diagnosis is assured. The finding of elastic tissue is an infallible sign, and will remove any doubt which may have previously existed. When defervescence in croupous pneumonia is atypical or retarded, or when chills and irregular fever occur after crisis has taken place, suspicion should at once be aroused as to the possibility of suppuration in the lung. If the sputum undergoes the characteristic changes, the suspicion will be strengthened and probably confirmed in course of time by rupture of the abscess.

The principal conditions with which abscess of the lung might be confounded are bronchiectasis and empyema. The former, although presenting some symptoms common to abscess, such as the expectoration of purulent sputum and hectic temperature, is to be differentiated by the history and absence of elastic tissue in the expectoration.

In purulent pleural effusion which has ruptured into the lung the physical signs of the primary disease will usually remain, so that dulness over the posterior pulmonary area increasing from above downward will be present, and the breath sounds over this area will be diminished. In some cases the symptoms and signs of pyopneumothorax supervene.

Diagnosis between an interlobar empyema and a pulmonary abscess which has not communicated with a bronchus is practically impossible, and even after perforation of the one and rupture of the other has occurred there may be nothing by which a differential diagnosis can be made.

It may be impossible to distinguish abscess from gangrene affecting a limited area of pulmonary tissue, although a horribly offensive odor of the breath and an extremely foul-smelling expectoration bespeak the existence of gangrene.

**Prognosis.**—Pulmonary abscess is a serious disease, but the prognosis depends in some degree at least upon the cause and upon the size and number of lesions present. Acute multiple abscesses due to septic emboli are always fatal. Abscesses due to foreign bodies are very fatal, while those due to penetrating wounds usually heal kindly unless a large area of tissue has been destroyed. In single abscess following croupous pneumonia hope for recovery should always be entertained. If the abscess ruptures, or can be evacuated by surgical intervention there is a fair prospect of recovery. Of course, the longer the abscess cavity persists the greater will be the danger of death from septic poisoning and exhaustion, from amyloid disease, and from hemorrhage due to erosion of vessels in the abscess wall.

Purulent pericarditis, abscess of the brain, and rupture into the pleural cavity render the prognosis more unfavorable. If surgical intervention can be practised at once in the latter occurrence the patient's chances of recovery will probably be increased, but unless operation is done at once, they are certainly diminished.

**Treatment.**—Medicinal treatment must be directed mainly to sustaining the patient's strength. For this purpose stimulants and tonics are indicated. Alcohol in the form of whisky or one of the stronger wines, such as port or tokay, should be given freely. Nutritious liquid food must also be supplied to the patient. Milk, eggs, strong broths, and cocoa are appropriate articles of diet.

Inhalations of carbolic acid have been highly recommended, but it is doubtful if they accomplish any good. In chronic abscess, iron and arsenic in addition to alcoholic stimulants will be found useful. It is in this class of cases, too, that antiseptic inhalations may prove of value. Carbolic acid, creosote, eucalyptol, and benzoin may be tried. They may stimulate the wall of the abscess and hasten healing. For excessive cough small doses of opium or codeine are permissible, but care must be taken not to give enough to check the secretions.

In small multiple pyæmic abscesses treatment is of no avail. In regard to the surgical treatment of pulmonary abscess, it may be stated that whenever an abscess can be located, and there is reason to believe that other foci of suppuration are not present, pneumotomy should be performed. The trend of modern surgery is to liberate pus wherever it may form, and this is a correct attitude. Although some pneumonic abscesses heal spontaneously after rupture occurs, it seems that they should invariably be opened and drained once they are positively located. By treating them in this manner the patient will be less exposed to such complications as empyema, purulent pericardial effusion, cerebral abscess, and septicopyæmia. When due to extension of suppuration processes originating outside the lung, for instance, to rupture of a subphrenic abscess or an empyema, operation is also urgently demanded. So likewise is it when an abscess breaks into the pleural cavity. Resection of one or more ribs as the case may necessitate, followed by free incision into the abscess and the introduction of a drainage tube, is a much more rational procedure than aspiration. In view of the present advanced technique of operating it can hardly be considered necessary to wait for the formation of pleural adhesions before completing the operation in cases in which they are not present.

## NEW-GROWTHS OF THE LUNG.

**Etiology.**—The etiology of primary tumors of the lung is enveloped in the mystery which surrounds that of new-growths in general. Primary cancer is much more frequent, 3 to 1 in men, and of West's 5 cases of primary sarcoma 4 were in men, the sex in the fifth case not being stated. This by inference is in harmony with Aufrecht's belief that trauma is of very great etiological importance. In each of his 4 cases of cancer there was a clear history of injury, and he cites similar instances from the experience of others. Workers in cobalt mines appear especially predisposed to pulmonary cancer.

**Morbid Anatomy.**—This depends largely upon whether the growth is benign or malignant, primary or secondary. In general, primary tumors are much less frequent than secondary, due either to metastasis or to extension from contiguous tissues. The primary are commonly unilateral, the secondary bilateral. The latter, when metastatic in origin, are often widely disseminated.

Benign tumors of the lung are very rare. Adenomata originating in the bronchial glands have been found. Of the connective-tissue series, osteoma, chondroma, fibroma, and lipoma are occasionally met; they are usually small and multiple. A true primary osteoma was reported by Virchow, but there seems little doubt that some so designated have been in reality calcific foci in tuberculous or other disease areas. A few cases of primary enchondroma are on record. They are small, multiple tumors originating from the bronchial cartilages, rarely exceed 1 cm. in diameter, give rise to no symptoms, and consequently are of pathological interest only. Of secondary osteoma and chondroma, 14 cases are on record. Fibroma is rare, as is also lipoma; the latter is sometimes found as small collections of adipose tissue between contiguous lobes.

Malignant tumors are sarcomas and carcinomas. The former is relatively rare as a primary tumor. Of West's 15 cases of sarcoma of the lung, 5 were primary in that organ. The endothelioma, or sarcoma derived from endothelial cells, is the most common primary malignant connective-tissue tumor. It usually originates in the pleura, but may spring from the lining cells of trabecular lymph spaces or bloodvessels. Of sarcomas secondary in the lung, those originating in bone are the most frequent, a third or more coming from this source. So far as the lung is concerned these tumors do not always conform to the general rule regarding age, and appear more often in adult or advanced life. In some cases there is a long interval between the appearance or removal of the primary tumor and the metastasis in the lung. Prentiss reports a case of removal of a sarcoma of the testicle with symptoms of secondary growth in the lung developing four years later, the patient living another year. Any of the histological types of sarcoma may be thus transmitted to the lung, but, as elsewhere, the round-celled variety is most frequently brought by the blood stream. Melanotic sarcomas also appear. Possibly belonging to this tumor group is the syncytioma, which occasionally develops in the lung as a secondary growth. Hypernephroma is also a metastatic tumor in the lung and pleura.

Carcinoma is the most frequent tumor of the lung and, while compared with sarcoma, a relatively large proportion are primary, the greater number even of cancers are secondary in origin. The primary is commonly encephaloid in type, although from the anatomy of the lung most secondary growths also, even if from a scirrhus, assume a very cellular structure. West particularly emphasizes the fact, however, that cancer of the root of the lung tends to become excessively fibrous. When primary the tumors may involve most or all of a lobe or an entire lung. In the latter cases tumors weighing as much as nine pounds have been found. Secondary foci may develop by dissemination of the original tumor. Perl, Malassez, Boix, and others, endorsed by Aufrecht, hold that true primary cancers of the lung take origin from the alveolar epithelium. The pulmonary tissue may be invaded, however, by tumors originating in bronchial mucous glands. Primary cancer may remain in the lung or extend to neighboring structures, including

the opposite lung. The tumor may appear externally, but extension through the chest wall is not a frequent occurrence. At times when a bronchus is invaded, the growth extends through the wall and appears as papillary masses projecting into the lumen. In these cases, possibly more often than when the growth is confined to the pulmonary alveoli, fragments or individual cells may be detached and expectorated; a few cases have been diagnosticated by finding these in the sputum.

Secondary cancer of the lung is commonly bilateral unless due to extension from contiguous tissues, these including the mediastinum, neck, chest wall, and through the diaphragm from abdominal structures. The possibility of extension from the parietal pleura without the intervention of adhesions is held by some writers. Metastasis by the lymphatics is a common source of these tumors, but cells are also brought to the lungs by bloodvessels. The latter method may give rise to relatively few small or large nodules in the interior and appearing as bossed or umbilicated elevations beneath the pleura, or to innumerable small, scattered foci; to the latter condition the term carcinosis of the lung has been applied. Cases of extension to the lung through the air passages of squamous epithelioma of the mouth or larynx have been observed.

The effect on the lung of all the varieties of malignant growths is much the same. According to their size they are substituted for a small or large part of the pulmonary tissue and exert pressure on all or a part of the remainder. The latter usually leads to compression and atelectasis of the tissue immediately bordering the tumor nodules, although as a whole the intervening lung, especially if the growth be extensive in the shape of multiple foci, is emphysematous. If the tumor affects a lobe or more as a single large mass, the remainder of the organ is sure to become overdistended. Congestion and possibly added œdema may occur in the pulmonary tissue surrounding the tumor nodules; under these circumstances hæmoptysis not infrequently results. Subacute inflammatory changes may also take place in the bordering tissue and in some instances lead to softening; in addition to or independent of this, the tumor itself may soften, the process in either instance resulting in cavity formation. Pressure on the blood and lymph vessels and on the bronchi by tumors at the root of the lung lead to secondary changes, as atrophy, necrosis, œdema, and atelectasis, such as would develop from like interference by other causes. Hydrothorax or pleurisy, the latter either serofibrinous or hemorrhagic, not infrequently complicate cancer or other malignant tumor of the lung.

**Symptoms.**—In considering the symptomatology of new-growths of the lung the benign tumors may be disregarded because of their rarity and also for the reason that when they are present they may not produce any disturbance. As carcinoma and sarcoma give rise to the same symptoms they may be considered together.

When these growths are secondary it sometimes happens that their evolution is so slow and the manifestations of malignant disease in other parts of the body so pronounced that evidence of pulmonary involvement is not detected during life, the lesions being discovered only upon autopsy. As a rule, however, especially when the tumors are primary, the disease manifests itself by well-marked, although by no means distinctive, symptoms consisting primarily of dyspnœa, cough, and expectoration.

Dyspnœa is constant and progressive. At first perhaps only of slight

degree or noticeable upon unusual exertion, it gradually becomes worse until in extreme cases it may amount to orthopnœa. It is especially severe in cases in which the neoplasm invades the mediastinum and presses upon the lower portion of the trachea. Interference with the circulatory area of the lung, invasion of the bronchi, and the pleural effusion all contribute to its production, but it is of course most intense when the trachea is compressed. Tumors which grow rapidly naturally produce dyspnœa more quickly than do those whose evolution is more gradual. Cough is variable, depending somewhat upon the size and location of the growth. Thus when a tumor is so situated as to compress the pneumogastric nerve the cough will be hard and dry, whereas if the tumor is disintegrating, or of an associated pneumonia be present, it will be freer and accompanied by expectoration.

Expectoration is variable both as to its quantity and characteristics. The sputum may remain mucoid or muco-purulent throughout the course of the disease, although it is often blood-stained, and has also been known to be of a bright-green color. Sometimes it is coughed up as clear-red, homogeneous masses, which have been compared to pieces of currant jelly. There is nothing significant about this sputum; it is merely a homogeneous admixture of mucus and blood, the two being so thoroughly blended that one cannot be distinguished from the other. Sometimes a little pure blood may be coughed up, and if the neoplasm extends into a large air cavity, free hemorrhage may result.

Particles of the tumor itself may also be expectorated. Hampeln has called attention to the presence in the sputum of unpigmented polymorphous cells of different sizes in which both nuclei and nucleoli show plainly. He believes that these cells are pathognomonic of cancer.

Other symptoms worthy of mention are pain, fever, hæmoptysis, dysphagia, interference with phonation, and disturbances of the circulation.

Intercostal pain is not uncommon, but it may not be so severe as to cause much distress. West mentions a case in which neuralgic pain extended down the inner side of the arm, it being due of course to pressure upon the outer costohumeral nerve. Herpes zoster sometimes runs along the course of a nerve thus compressed. When the pleura is involved intense pain may be a constant symptom.

Fever is present in some cases, and Fränkel observed it in 19 out of 35 cases. It no doubt is often due to associated suppurative processes in the lung, but it also has been attributed to resorption of the tumor elements.

Pressure of the growth upon the œsophagus causes dysphagia. If the recurrent laryngeal nerves be compressed disturbances of phonation such as hoarseness, inspiratory stridor, and aphonia will result; pneumogastric compression may cause cardiac disturbance, such as irregularity of the pulse. Pressure upon the sympathetic will give rise to inequality of the pupils and flushing of one side of the face. If the growth encroaches upon the large bloodvessels in the lung, circulatory disturbances will also be produced. If the superior vena cava is involved, symptoms of cerebral congestion, such as dizziness, headache, epistaxis, or even meningeal hemorrhage, are likely to supervene. Further reference to this class of circulatory disturbances will be made when we come to consider the physical signs.

In regard to cachexia, it may be stated as a rule that it develops more slowly and is not so pronounced in primary malignant disease of the lungs as it is in other forms of cancer and sarcoma.

**Physical Signs.**—The physical signs of new-growths of the lung depend upon their size and situation and upon the condition of the surrounding pulmonary and other contiguous tissues. Thus, when a considerable area of lung is involved by an extensive infiltrating mass the signs will be different than when only a few small, isolated nodules are present. Again, when bloodvessels are compressed or elevated by the neoplasm, manifestations on the part of the circulatory system will be observed which are absent when the tumor is so situated as not to impinge upon the vessels.

Upon inspection, changes in the shape of the thorax may be noticed. In case there is a large infiltrating growth in the lung the corresponding side of the chest may bulge out and the intercostal spaces be widened. A pleural effusion may also cause bulging. On the other hand, when collapse of the lung has taken place as the result of bronchial occlusion, the thorax may be retracted and its circular measurement considerably diminished. The affected side of the thorax does not move with respiration.

When the neoplasm presses upon the superior vena cava, considerable distention of the superficial cervical veins will be seen. If the pleura be involved in such a manner that the caliber of the internal mammary vein is diminished, owing to the compression to which it is subjected, the superficial veins of the chest will be unduly filled and stand out prominently under the skin.

Palpation shows that vocal fremitus is normal or exaggerated, according as the growth is localized or diffuse. Percussion elicits variable sounds which depend upon the extent and character of the neoplasm and the condition of the parts around it. In diffuse infiltration of the lung, dulness may be elicited over a considerable area of the thorax. Areas of atelectasis as well as patches of pneumonic infiltrate around a softening and isolated nodule near the periphery of the lung may also give forth a dull note. As a rule, however, isolated nodules in the early stages of their evolution do not cause any changes in the normal percussion note. Sometimes resonance may be slightly impaired or perhaps a hyperresonant note may be obtained. Hyperresonance is often heard when a bronchus becomes obstructed; when a cavity is formed by disintegration of the neoplasm and inflammatory softening of adjacent tissue, an amphoric note will be emitted over the area covering the cavity.

The results of auscultation are likewise variable. In extensive infiltration the breath sounds are much diminished, or may even be absent, being replaced by bronchial breathing. In the nodular form of the disease, however, very slight alterations will be detected. The breath sounds may be somewhat diminished in intensity and perhaps a little rough. Associated pulmonary congestion or œdema, as well as bronchitis, give rise to rales of various kinds. In case a cavity is present cavernous breathing and pectoriloquy may be heard. The cardiac sounds are often abnormally distinct, being transmitted through areas of solidified tissue.

**Complications.**—The chief complications of malignant disease of the lungs are pleurisy, pneumonia, gangrene, and atelectasis.

The pleura may be attacked by the malignant growth, with the result that it becomes much thickened and indurated. Effusion into the pleural cavity is not at all uncommon when such involvement is present, and the fluid is very likely to be sanguinolent. Rarely, a purulent effusion may be present. Pneumonic consolidation and œdema of the lung are sometimes

observed in the course of malignant disease; the latter no doubt is in many instances due to pressure of the growth upon the pulmonary veins, although it may result from stasis in the smaller vessels. Gangrene may ensue either as a result of the destructive process itself or may follow occlusion of blood-vessels by the pressure of the neoplasm upon them. Atelectasis is not at all uncommon, owing to occlusion of the bronchi. Metastases in other parts of the body—the liver, kidneys, and joints, for instance—sometimes occur. Distinct enlargement of the supraclavicular glands may be noticed.

A very few cases have been reported in which a cancer of the lung has perforated externally, but such an occurrence is exceedingly rare.

**Diagnosis.**—The diagnosis of new-growths of the lung may be very difficult if the tumor is small and situated deep in the lung. Even when several such isolated nodules exist, characteristic symptoms may not be manifested and the physical signs may be similar or identical with those observed in other pulmonary disorders. Metastatic growths are very liable to escape attention, especially if they occur late in the course of the primary malignant disease. Pulmonary symptoms associated with emaciation and cachexia, supervening after the removal of a malignant growth in another part of the body, would naturally arouse suspicion, although there may be nothing upon which to make a positive diagnosis.

In other cases where the malignant process is extensive and contiguous, and perhaps even remote structures are involved, diagnosis will be readily made. A combination of such characteristic phenomena as dyspnœa unassociated with cardiac disease or severe bronchitis, mediastinal compression, enlargement of the supraclavicular glands, expectoration of currant-jelly sputum, together with the physical signs of pulmonary consolidation or excavation, will leave little or no doubt as to the nature of the affection with which we have to do. The finding of particles of tumor in the sputum would of course make diagnosis positive.

Cases in which there is early involvement of the pleura may be most difficult to recognize. Bulging of the thoracic wall may be caused either by a tumor or by an accumulation of fluid in the pleural cavity, but when it is due to the former cause the tumefaction is apt to be more irregular than when it results from the latter. An encysted empyema, however, might give rise to a localized bulging in the side, and is therefore to be borne in mind. In tumor the dulness may extend from above downward, a condition quite the reverse of that which obtains in pleural effusion. In tumor, moreover, dulness is often not uniform in different parts of the chest, whereas in pleurisy with effusion there is little variation in its degree of intensity unless the patient changes his position and thereby causes displacement of the fluid.

Thoracentesis affords valuable aid in clearing up the difficulty. In some cases the exploring needle may be carried through a much thickened pleura and then fail to withdraw any fluid; this circumstance points strongly to malignant disease, and even although fluid finally be reached the thickening is suggestive of malignancy. If shreds of tissue which adhere to the exploring needle prove to contain carcinomatous or sarcomatous cells, the suspicion will of course be converted into positive knowledge. When fluid is obtained its character may serve to elucidate the nature of the malady. As already stated, in malignant disease it is apt to be hemorrhagic. The presence of a sanguinolent effusion, however, must not of itself be con-

sidered conclusive evidence of malignant disease, for it sometimes occurs in tuberculosis and renal disease. Taken in conjunction with the associated symptoms and signs, however, it is of value. The presence of cancerous elements in the effusion, as revealed by microscopic examination, is of course conclusive. Not so much value is to be attributed to the finding of fat for the reason that it sometimes is present in tuberculous affusions.

Neoplasms of the lung which produce mediastinal compression may give rise to symptoms some of which are identical with those produced by aneurism of the aorta. Thus in both affections dyspnœa and stridor will be prominent manifestations of the pathological changes in the organism. Moreover, when a tumor is so situated as to elevate the great vessels distinct pulsation may be felt, and circulatory disturbances may also be produced. The most valuable point of differential diagnosis is constituted by the fact that when an aneurism attains sufficient size to produce symptoms it will form a pulsating tumor directly over or very close to the heart. From this pulsating area a dull percussion note will be emitted. In aneurism there is no enlargement of the supraclavicular glands, and, moreover, changes in the sputum such as may occur in malignant disease of the lung are not present. The fluoroscopic examination is frequently of great assistance. A new-growth does not show the expansile pulsation of an aneurism.

New-growths of the lung may be confused with tuberculosis. Thus when a few small, isolated, primary nodules undergo softening, with the result that cavities are formed and hemorrhage takes place owing to erosion of vessels, the disease may be mistaken for a beginning pulmonary tuberculosis. If it happen that a small hyperresonant area be discovered in the upper anterior region of the thorax, the error is likely to be more firmly fixed in the physician's mind. The presence of fever in such cases lends aid to the mistake, as do likewise the existence of rales produced by inflammation around the area of disintegrating tissue. In such cases the age of the patient will afford some assistance in guiding the physician to a correct understanding of the malady. Such hemorrhage occurring in a person past middle life should direct attention to the possibility of cancer or sarcoma. In malignant disease, enlargement of the supraclavicular lymph glands will generally be found, whereas in tuberculosis their size will probably not be increased. Examination of the sputum, if carefully conducted, will in course of time decide the question.

**Prognosis.**—Malignant disease of the lung is of course incurable. Death may result from asthenia, asphyxia, hemorrhage, gangrene, or œdema. In regard to the duration of life no adequate data are obtainable, for the reason that there is no way of determining at what time the disease begins. Some patients die within a few weeks or months after the first manifestation of symptoms. Others may live for a year or two.

**Treatment.**—All that can be done is to relieve symptoms and endeavor to sustain the patient's strength. Morphine and cannabis indica should be used freely to control pain. Oxygen may be administered for dyspnœa, but when the latter is excessive and due to compression of the trachea, little good can be expected to follow its use. Operative treatment offers no hope of success. If a primary growth could be recognized early it might be successfully removed, provided it were small and superficially located; but in our present knowledge it is impossible to make a diagnosis sufficiently early to enable us even to entertain any thought of surgical intervention.

# CHAPTER XX.

## DISEASES OF THE PLEURA.

By FREDERICK T. LORD, M.D.

### PLEURITIS.[1]

**Historical.**—The term "pleuritis" was in use previous to the time of Hippocrates, but designated any febrile disease accompanied by pain in the side, and thus included disease of neighboring organs as well as the pleura. Hippocrates and Galen separated peripneumonia from pleuritis, which was regarded as an affection of the costal pleura alone. Boerhaave was the first to establish the site of pleurisy exclusively in the pleura, a view which Van Swieten shared, while Sydenham, Haller, and Morgagni believed that both lung and pleura were often, if not always, involved together. Pinel was the first to class pleuritis definitely as an inflammation of the serous membranes and to regard it as an independent disease, from the anatomical lesions. Laennec's masterly account of pleuritis and its recognition laid the foundation for our present knowledge, and since his time little advance has been made in diagnosis by physical signs. More accurate anatomical and pathological knowledge has led to a better understanding of the relation between diseases of the lung and the pleura, of the value of thoracentesis, of the importance of tuberculosis in pleurisy, and of the diagnostic value of various forms of cells in pleural fluids.

**Thoracentesis.**—The evacuation of pleural fluid by operation dates back to a remote and uncertain period. The legend runs, as Cicero and Pliny relate, that the suggestion of operation had its origin in the wounding of Pheraeus who, told by his physicians that he had an incurable ulcer on the lungs, exposed himself in battle that he might be slain, but the enemy's weapon pierced his side, allowing the pus to escape, and he recovered.

Galen states that the life of Cinesias was saved by Euryphon, of Cnidus, who opened the chest with the actual cautery. The operation was frequently performed in the time of Hippocrates. The diagnosis was made from observation of the breathing, fever, pain and cough, succussion sounds, the position of the patient, and swelling of the side. Evacuation was accomplished by the actual cautery, the knife, and perforation of a rib. The operator

[1] The statistical data on pleuritis are from three sources: (1) The Massachusetts General Hospital (M. G. H.), Boston; (2) the Presbyterian and (3) Roosevelt Hospitals, New York.

The writer is greatly indebted to W. B. James, of New York, for his kindness in placing much valuable data on diseases of the pleura at his disposal. The M. G. H. data were in great part gathered by C. L. Overlander. The hospital records are rich in data on the cytology of pleural fluids, much of the work on which was done by P. Musgrave.

is cautioned to prepare for operation by washing the patient with warm water. Celsus and Galen employed the operation, but it was regarded as dangerous and was largely given up among the Greeks and Romans. In the sixteenth century the operation was again recommended, among others, by Ambroise Paré, but was seldom done except in extreme cases. It was often practised in the seventeenth and eighteenth centuries, but had many opponents, and was usually unsuccessful. Dupuytren had only 4 recoveries in 50 cases, and himself died of empyema, saying of himself that he would rather die by the hand of God than of man. Druin, about the year 1665, proposed the use of the trocar as a substitute for the actual cautery in opening the chest. Aspiration was employed by Scultetus in 1669. An incision was made with the knife, and by puncture with the sharp cannula. Suction was applied by the mouth, by cups, and by syringes.

The great improvement in the diagnosis of thoracic disease following Laennec's publications did not exert an immediate influence on the question of thoracentesis, but finally overcame previously existing indecision. Laennec, himself, was not an earnest advocate of operation, and states that he never obtained any lasting success by its use. He recommended operation in acute pleurisy with fluid accumulation, when at the end of some days there is danger of suffocation; and in chronic cases, where other means have failed. He advised puncture with the trocar when, owing to weakness, the total evacuation of the fluid may cause dangerous syncope or as a means of alleviation in hopeless cases.

Among others in Germany, Becker (1834), Schuh and Skoda (1841), and Wintrich (1854); in France, Trousseau (1843), Marotte (1854), and Sédillot (1855); and in England (1844), Hughes and Cock, Roe and Thompson, advocated thoracentesis. In America at this time the general opinion was against the procedure. As Bowditch wrote in 1851, the operation "is strongly advocated by a few and as strongly opposed by others, and looked upon with indifference by the great mass of European physicians."

In 1849 or 1850, H. I. Bowditch,[1] who had long been impressed with the necessity of operation for pleural fluids, was confirmed in this opinion by the paper of Hughes and Cock. In 1850, he saw a case which, in his opinion, demanded tapping, and called Morrill Wyman in consultation. The operation was done by Wyman, who used an instrument devised by him, consisting of an exploring trocar to which was attached a strong suction pump. From this time Bowditch became an earnest advocate of aspiration, and by his publications did more than any other to introduce the method into practice in America and Germany. His conclusions as to the indications for operation are of historical interest, and very nearly represent the opinion of the present day, viz., to operate in acute or chronic cases where the chest is full and distended with fluid, even without dyspnœa; where there is alarming or paroxysmal dyspnœa, even if the chest be only partially filled with fluid; in all *acute* cases where the remedies employed do not produce ready absorption, and, "furthermore, as it may be of service in relieving dyspnœa and helping on the more rapid cure, it may, therefore, become a question whether even a small quantity of fluid should not be removed within a week after the first attack of acute pleurisy."

The apparatus for aspiration has undergone certain important modifi-

[1] *American Journal of the Medical Sciences*, 1852.

cations. In 1858, Thompson[1] described a lateral outlet from the body of the cannula. This was modified by Fraenzel[2] in 1874 by adding a stopcock in the lateral outlet and a device for preventing the entrance of air into the body of the cannula when the stylet is withdrawn. In 1869, Dieulafoy devised an aspirator consisting of a fine needle connected by a rubber tube to an apparatus in which the air can be exhausted. In 1872, Potain and Castiaux, in Paris, and von Rasmussen, in Copenhagen, suggested the bottle aspirator in which negative pressure is maintained by an air pump. Dieulafoy's rack aspirator and Potain's bottle method are still much in use. By the use of these instruments the entrance of air into the pleural sac during aspiration is prevented, thus obviating the danger of artificial pneumothorax and possible infection of the pleura.

Aspiration in both serous and purulent effusions was at first a common practice, but aspiration is now generally restricted to other than purulent fluids and free incision is used for empyema.

**Occurrence.**—From the point of view of the pathologist, the occurrence of pleuritis is very frequent. Including simple adhesions with other more marked changes in the pleura, pleuritis was found in 160 (74.4 per cent.) of 215 cases at autopsy (M. G. H.). Such processes pass unheeded or undiagnosed in the great majority of patients, as is shown by the striking disparity between autopsy and clinical reports. Thus, of 18,543 patients admitted to the medical wards of the Massachusetts General Hospital from 1897 to 1906 inclusive, only 460 (2.4 per cent.) are recorded as suffering from pleuritis. Fraley's[3] figures for the Pennsylvania Hospital are nearly the same: 505 (2.5 per cent.) in 19,396 cases. Gerhardt reports 3.47 per cent. of cases with pleuritis in Würzburg among medical patients during thirteen years, and 0.9 per cent. in eight years at the Charité in Berlin. Uncomplicated inflammation of the pleura is not a frequent cause of death. Thus, of 2,642,555 deaths recorded in the *U. S. Census Report* for five years (1900 to 1904), only 7420 (0.2 per cent.) are assigned to pleurisy.

**General Etiology.—Age.**—Pleuritis has been described in the newborn, but is relatively uncommon in infants. Wrany (quoted from Gerhardt) noted pleuritic adhesions in infants of fifteen days and three weeks. Holt states that the youngest case in which he has found extensive pleuritic adhesions is in an infant of three months. Baron[4] found evidence of pleuritis in 159 of 403 autopsies on children. Pleuritic effusions in children are more often purulent and metapneumonic in origin, while in adults serous and tuberculous pleuritis is more common.

The relation of age differs somewhat between clinical and mortality statistics. Of 760 clinical cases (M. G. H.)[5] of different forms of pleuritis, 63 were ten or under, 114 eleven to twenty, 255 twenty-one to thirty, 178 thirty-one to forty, 83 forty-one to fifty, 51 fifty-one to sixty, 12 sixty-one to seventy, while 4 were seventy-one to eighty. Thus, about one-third of the cases occurred from twenty-one to thirty and more than one-half from twenty-one to forty. In mortality returns, the cases are much more evenly distributed through the different ages, with a larger proportion at the extremes

[1] *Medical Times and Gazette*, 1858, p. 329
[2] *Berliner klin. Wochenschrift*, 1874, xii.
[3] *American Journal of the Medical Sciences*, May, 1907.
[4] *Journ. f. Kinderkrankheit*, i, p. 20.
[5] Children comprise only a small number of the total admissions.

of life. Of 7420[1] cases in the *United States Census Report* for five years (1900 to 1904) certified as dying from pleuritis, there are 997 under five (302 under one), 425 from five to fourteen, 755 from fifteen to twenty-four, 938 from twenty-five to thirty-four, 974 from thirty-five to forty-four, 1897 from forty-five to sixty-four, and 1415 sixty-four or over. These figures suggest that pleuritis is less common but more fatal at the extremes of age.

**Sex.**—In general, males are much more frequently affected. In the writer's series of 1681 patients with fibrinous, serofibrinous, or purulent pleuritis, 1213 were males, 468 females. In the *United States Census Report* (1900 to 1904) there were 4251 males, 3169 females. There appears to be no striking difference in the relation of sex at the different ages or in the different forms of pleuritis, males in general exceeding females.

**Occupation.**—The relation between pleuritis and occupation may be considered to be that of the diseases to which pleuritis is most often secondary. Thus, occupations predisposing to pulmonary tuberculosis or other respiratory infections may indirectly lead to pleuritis. As in tuberculosis, its influence is largely referable to poverty, poor ventilation, overcrowding, a low rate of wages, and, perhaps most important of all, ignorance in the disposal of infected material. Those occupations in which there is the greatest amount of dust, aiding in the distribution of expectorated bacilli, may most often be expected to lead to tuberculous pleuritis. The tabulation of occupation and pleurisy with effusion in 279 cases (M. G. H.) shows that dusty employment obtained in 60 (21.5 per cent.).

**Season.**—Since respiratory infection occurs more often during the colder months of the year, and because of the frequent association of pulmonary and pleural infection, we should expect a similar relation with the seasons to obtain in pulmonary and pleural infection. This has been shown to be the case. It is confirmed by the writer's 762 patients, of whom 248 (32.5 per cent.) sought the hospital clinic during March, April, or May, the greatest number of cases for any month being 94 in March; while 189 (24.8 per cent.) presented themselves in June, July, or August, 178 (23.3 per cent.) in December, January, or February, and 147 (19.2 per cent.) in September, October, or November.

**Exposure.**—With the growth of knowledge concerning the role of bacteria in the disease, exposure has come to be regarded as of little moment as a principal cause. It cannot, however, be totally disregarded, but must be looked upon rather as a contributing factor in certain cases. It is probable that in some unexplained way it favors the development of organisms already present in the respiratory tract. Of 467 cases of fibrinous and serofibrinous effusion it was a possible contributing cause in 34 (7.2 per cent.).

**Bacterial Etiology.**—As yet it is impossible to separate the inflammations of the pleura into sharply defined groups according to their bacterial etiology, with a characteristic clinical picture, pathology, course, and termination. Fibrinous, serofibrinous, or purulent pleuritis may be due to one or more different organisms in the same or in different cases. The number of organisms concerned is comparatively small, and in the great majority of cases comprises the tubercle bacillus, the pneumococcus, or the streptococcus. Pleural fluids, from the readiness with which they can be obtained for exami-

[1] Age unknown in 19 cases.

nation, are the most promising field for investigation, but fluids, in other respects similar so far as our present methods go, may show different bacteria.

The limited number of different organisms concerned is probably due to the relation of the pleura to the deeper parts of the respiratory tract, where mixed infections are less common. The tendency of the tubercle bacillus to invade the subpleural tissue or the thoracic glands in close relation with the pleura is well known, and explains its frequent invasion of the pleura.

**Tubercle Bacillus.**—This is a frequent cause of pleuritis, either alone or in combination with other organisms, but it is not yet possible with any degree of accuracy to state in what proportion of cases it is a factor in the different forms. It is undoubtedly one of the most common but not the only cause of fibrous adhesions and scars so commonly found in the pleura and most often at the apices. In many instances these are the result of extension of inflammation about tuberculous foci, evidence for which is afforded by the presence in the underlying pulmonary tissue of caseous, fibrocaseous, or calcified areas. When not so associated, they cannot be regarded as necessarily tuberculous in origin, and may arise from preceding inflammation due to other organisms. The tubercle bacillus with other organisms is at times undoubtedly a cause of fibrinous pleuritis, and tubercles may be found in such tissue. The failure to find other organisms than the tubercle bacillus in purulent pleural exudates does not establish their independent relation with the latter, for other organisms may have been present and died out.

The tubercle bacillus plays a most important part in serous effusions, in which it has been demonstrated in from 22 to 85 per cent. by different observers as a contributing or principal cause. At present we have no certain means of excluding it, and it may still exist even with negative inoculation experiments.

**Pneumococcus.**—The pneumococcus may be a cause of fibrinous, serofibrinous, or purulent pleuritis. It is a common factor in the fibrinous form. It is only rarely a cause of clear serous effusions, but is more common in turbid exudates and is frequent in purulent effusions. It is common in the primary empyemas of children and in all effusions complicating lobar pneumonia.

**Streptococcus.**—This is less common in serofibrinous exudates than the pneumococcus, but is not infrequently present in empyema. It is common in suppurative pleuritis secondary to such diseases of the lung, as lobar pneumonia and bronchopneumonia, abscess, gangrene, bronchiectasis, following trauma to the chest wall or septic processes in more remote parts of the body.

**Other Organisms.**—*Staphylococcus pyogenes aureus* is, perhaps, the next most common organism found in pleural exudates. *Streptococcus capsulatus*, influenza bacillus, Friedländer's bacillus, diphtheria bacillus, *Micrococcus tetragenus*, *Bacillus ramosus*, *Bacillus pyocyaneus*, and *Bacillus subtilis* have been occasionally found, either alone or in combination, and at times associated with the tubercle bacillus, the pneumococcus, or the streptococcus in purulent exudates. The typhoid bacillus has rarely been cultivated from pleural fluids of a serofibrinous, hemorrhagic, or purulent character. The demonstration of an organism with the morphology, staining reaction, and cultural peculiarities of the gonococcus is reported by Bordoni-Uffreduzzi.[1] The cultures are not described.

[1] *Deutsch. med. Wochenschrift*, 1894, Nr. 22.

**Classification.**—It is impossible at present to classify the inflammations of the pleura satisfactorily according to their etiology. The most convenient and practical division is into acute and chronic pleuritis, each of which may be primary or secondary, and according to the clinical or pathological findings, fibrinous, serofibrinous, or purulent. The terms "primary" and "secondary" are convenient for the description of clinical cases, but are somewhat misleading and need a word of explanation. Pleuritis is in reality only very rarely primary, almost always secondary to disease of neighboring organs, especially the lung. When cases are referred to as primary, therefore, it should be understood that the starting point of the disease in other organs has not been detected. Throughout the sections on effusions, frequent mention is made of small, medium, and large amounts of pleural fluid. In general, by "small" may be understood an effusion which does not rise above the angle of the scapula; by "medium," an upper level between the angle and spine of the scapula, and by "large," a higher level.

## Acute Fibrinous Pleuritis.

**Fibrinous or Plastic Pleuritis.**—The examination of cases with fibrinous pleuritis at the postmortem table shows that small amounts of fluid are usually present. From its clinical importance, however, the group deserves separate consideration.

**Etiology.**—The absence of fluid for examination makes the etiology of fibrinous pleuritis somewhat less certain than the other forms, but the cases fall into two principal groups, those in which the disease is apparently (1) primary and those (2) secondary to disease of the lung or other part of the body.

1. **Primary.**—This forms the largest group in clinical cases. The disease seldom occurs in perfectly healthy individuals, and some disturbance of the respiratory tract may precede, but more often accompanies, the stitch in the side. In the writer's series, 223 (64.6 per cent.) of 345 cases may be regarded as belonging to this class. Exposure was a possible contributing factor in 30 and alcoholism may have played a part in 19 cases. Undetected pulmonary or other tuberculosis is a probable contributing or principal cause in a considerable but uncertain proportion.

2. **Secondary.**—The disease may be secondary to infective processes in any part of the body. Disease of the lung occupies first place and bronchitis is an important factor. It is probable that small areas of pulmonary invasion, too small to be detected on physical examination, frequently accompany bronchitis, and that bacteria find their way from the peripheral parts of the lung to the pleura. Infection with the tubercle bacillus, especially in the lung or bronchial lymph glands, may be regarded as the starting point of pleural infection in a large proportion of cases. In this series there was probable or certain pulmonary tuberculosis in 18 cases (5.2 per cent.), of which 6 showed tubercle bacilli in the sputum. The lung was involved in 16, tuberculous peritonitis was present in 1, and an anal fistula in the remaining patient. Lobar pneumonia is a frequent cause and is represented by 15 cases. Bronchopneumonia, abscess, gangrene, and bronchiectasis are less frequent causes. Of infections in more remote parts of the body may be mentioned acute or chronic endocarditis, tonsillitis, pyorrhœa alveolaris,

arthritis, pericarditis, typhoid fever, and uterine sepsis. Dry pleurisy is not infrequent in the later stages of all chronic diseases accompanied by asthenia and increased susceptibility to infection. Trauma with or without gross injury of the tissues may lead to fibrinous pleuritis and usually by infection from the lungs. Stinzing[1] regards tertiary syphilis as an important cause.

*Relation to Tuberculosis.*—The frequency with which pulmonary tuberculosis begins with and is accompanied by symptoms referable to the pleura gives ample testimony of its important relationship. Of 1000 cases in the Winyah Sanatorium, 201 had pleurisy prior to the onset of pulmonary tuberculosis (von Ruch). Although the apical localization of these changes is most frequent, pulmonary tuberculosis is often accompanied by similar processes in other parts of the pleura. Acute fibrinous pleuritis may occur and tubercles may be found in the tissue.

The proportion of cases in which the tubercle bacillus is responsible for fibrinous pleuritis cannot be definitely stated. A study of the writer's cases suggests that this form of pleuritis as an apparently primary affection is tuberculous in about the same proportion of cases as in primary serofibrinous pleuritis. This seems to be indicated by the subsequent course. (See Prognosis.) It should be noted, however, that coincident tuberculosis was demonstrated in a smaller proportion of cases of fibrinous (5 per cent.) than of serofibrinous pleuritis (13 per cent.). The tuberculin reaction was less often obtained. Of 12 cases of fibrinous pleuritis in which it was tried, a reaction was obtained in 4 (33.3 per cent.), while of 47 patients with serofibrinous pleuritis, in 36 (76.5 per cent.) the test was positive.

Although the tubercle bacillus may be equally responsible for fibrinous and serofibrinous pleuritis, there is some indication that a mixed infection with other organisms is more frequent in the former. An abundant fibrinous exudate is not typical of infection with the tubercle bacillus alone. The behavior of the white count is also suggestive of mixed infection, being above 12,000 in 19 (39.5 per cent.) of 48 cases of primary fibrinous pleuritis, while only 3 (9.09 per cent.) of 33 cases of primary serofibrinous effusion, known to be tuberculous, exceeded this figure.

**Special Pathology.**—The inflamed pleura lacks its normal lustre, is dull, opaque, and coarsely or finely granular, an appearance which can best be seen by scraping the tissue with the knife. It is grayish white, or reddish, and deeper red in places where ecchymoses are present. The membrane is thickened and may reach a centimeter or more in width. The surface of an abundant exudate may be thrown into folds or projecting masses of various shapes. The amount of exuded liquid varies. There is practically always more than the normal amount of pleural fluid and this is usually cloudy. The extent of pleural involvement varies from a part to the whole of the pleura. It is not uncommon to find some extension of the inflammation along the interlobular septa in cases with severe fibrinous pleuritis.

On microscopic examination, desquamation and degeneration or absence of epithelial cells are found. The subserous tissue is swollen and contains an increased number of polynuclear cells. Lymph and blood-vessels are widened. The surface of the pleura is the site of a fibrinous layer containing numerous pus cells and serum. With the beginning of

[1] *Handbuch der Therapie inneren Krankheiten*, 1902, Band iii.

resolution the fibrin undergoes fatty metamorphosis and in mild cases may entirely disappear. In more severe inflammations the two layers of pleura become adherent. Organization, round-celled infiltration, and connective-tissue formation take place, giving rise to adhesive pleuritis.

**Site.**—This is variable, but the process is most often discovered clinically in the lower lateral and anterior aspects of the chest. This is due to the more frequent occurrence of fibrinous pleuritis at the bases, the greater respiratory excursion of the lower part of the lung, increasing the loudness of friction sound, and the relative thinness of the thoracic wall, facilitating the detection of pleural processes here. The more frequent discovery of pleural friction in the lateral and anterior rather than in the posterior part of the chest may also be due to the tendency of small amounts of fluid to collect at the base posteriorly, with mechanical limitation of pulmonary motion and slight intervention of fluid between lung and chest wall in this region. Of 323 cases in which the site of the process was noted in this series, it was on the right in 134 patients, in 131 on the left, while the process was limited to the right upper chest in 20, to the left upper in 9. Of the remaining 29 cases, a situation at both bases in 7, in the diaphragmatic pleura in 3, and throughout the left side in 1 may be mentioned.

**Symptoms.**—Prodromata are relatively uncommon. Cough and expectoration, due to respiratory infection, may precede the stitch in the side. In a majority of the cases the onset is sudden, with pain, which varies much in intensity. An initial chill is rare. The temperature is often not elevated and was not above normal in 82 (23.7 per cent.) of 345 cases. A temperature of 99° to 100° or 101° is not uncommon. It may rise to 103° or higher, but high temperature is more often seen in complicated cases. Fever, if present, usually gradually subsides within a few days.

**Pain.**—Pain is an almost constant feature. It may be absent after the acute symptoms have subsided or at the extremes of age. It is often described as sharp, stabbing, or cutting, sometimes dull and dragging in character. It is usually circumscribed, rarely diffuse, and is felt in the axillary or mammary region, less commonly in the anterior or posterior lateral and lower parts of the affected chest. It may radiate to the shoulder or lumbar region, less commonly into the upper extremity, the neck or abdomen. The rare cases in which the pain is at first referred to the abdomen are troublesome for diagnosis. Of 145 cases in the writer's series this occurred in 8 (5.5 per cent.), and may have been due to diaphragmatic pleurisy. Pleuritic friction may be absent and the case may then present the picture of an acute abdominal affection. The pain is usually in the upper abdominal region. It may be accompanied by tenderness and muscular spasm and suggest an inflammatory abdominal condition. Indeed, laparotomy has occasionally been performed in cases in which a few days later the pleuritic origin of the symptoms became obvious from the presence of friction or effusion.

The pain of fibrinous pleuritis is usually of moderate intensity, at times almost unbearable, at others slight, and present only with long breath or cough. It may be continuous or intermittent, but is usually most marked at the beginning of the illness, disappearing suddenly or gradually within a week to ten days. In some cases it may last for weeks or months. Movement, laughter, pressure or percussion on the affected side, quick change of position, even elevation of the arm, may start or aggravate it. With the advent of pleural effusion, pain diminishes or disappears. The cause of

pain in pleural disease is uncertain. It is probably due to irritation of terminal nerve filaments in the inflamed tissue.

**Cough.**—This is present in a large proportion; of 145 patients it was noted in 103 (71 per cent.). It was stated to be absent in 18, and the records are silent on this point in 24. It is usually ascribed to pleural irritation, and a relation with this is suggested by the frequency with which forced respiration excites cough, and by its relief when the side is immobilized. Experimentation in animals has failed to confirm this supposition, but it may be that animals are less susceptible to pleural irritation. It is not improbable that pulmonary infection plays a part in its production, for in 44 cases (30.3 per cent.) expectoration accompanied the cough and rales were noted in 45 (31 per cent.). The sputum lacks characteristic features. It was muco-purulent or purulent in many. In 6 cases it was bloody.

**Dyspnœa.**—Quick respiration may exist without dyspnœa. When it occurs, dyspnœa is usually slight. It may be due to fever, an effort on the part of the patient to limit the excursion of the lung, because of pain; and if an effusion co-exists, it may be due to this.

**Physical Signs.**—The position, if confined to the bed, is inconstant; at times some relief is afforded by lying on the affected and at other times on the unaffected side. The patient is often more comfortable with the upper part of the spine deflected toward the diseased pleura and the shoulder of that side depressed, from the fixation and compression which this position affords. A diminished expansion and elevation of the involved side can be seen as well as felt, most often in the lower lateral thoracic region. The pulmonary excursion, as shown by percussion of the lower pulmonary margin at the end of inspiration and expiration, and by the amplitude of the diaphragm phenomenon, is usually diminished for both lungs, much diminished or absent on the affected side, and the interspaces are slightly narrower. Percussion may be painful. A change in the percussion note may be determined. The respiratory murmur is diminished but vesicular in character; the vocal fremitus may be diminished, but is usually unchanged.

**Pleuritic Friction.**—A friction rub can be heard and not infrequently felt as early as twelve to twenty-four hours after the onset of the process. Its occurrence and resemblance to the creaking of leather did not escape Hippocrates. It is often jerky and may be inconstant, present during one, absent at the next respiration, such irregularity being due to alternate fixation and motion of the visceral against the parietal pleura. It may disappear during the course of the examination. The rub is more distinct during inspiration than expiration. Fibrinous pleuritis may exist without friction sound, and friction does not exclude fluid in a neighboring part of the pleura. The sound is not pathognomonic of pleuritis.

**Pseudo-pleuritic Friction.**—Rosenbach mentions a rubbing or creaking sound which may closely resemble the true pleuritic friction, heard most frequently over the lower portions of the lateral wall, over the suprascapular fossa or in the interscapular space, and rarely in the supraclavicular fossa. He regards it as a muscular sound and as a frequent source of error. The writer has frequently heard this sound. It can often be brought out by asking the patient to breathe deeply for a considerable period. It begins as a faint rumbling, grating, low-pitched murmur, at first confined to inspiration, becoming more and more intense, and finally occupying both phases of respiration. It may become harsh and grating and hardly to be

distinguished by its quality alone from pleuritic friction. It varies in intensity in different patients, and during the course of the examination of the same patient, usually increasing for a time, then gradually fading away, but it may be reproduced after an interval of quiet; and may be heard at subsequent examinations of the same patient. It is much less jerky than pleuritic friction and rougher than the sound heard over any contracting muscle of the extremities. It is often bilateral, but in the writer's experience is heard more frequently over the scapulæ and more often on the left. It may be present in the anterior thoracic region, but less commonly than in the back. It may at times be palpated with the hand and may be audible several inches from the patient's side. It may be appreciated by the patient as a grating sensation, but causes no pain. It is present after cough. Firm fixation of the shoulders, the scapulæ, and the side do not serve to abolish it. The writer is disposed to regard it as due to the rubbing of the two pleuræ together in the absence of sufficient pleural secretion.

**Pleuro-pericardial Friction.**—This is not infrequent and is often difficult of interpretation. It may be due to inflammation of the pulmonary, costal, or that part of the mediastinal pleura overlying the heart. Pleuritis in the cardiac region is likely to be influenced by the movement of the heart as well as by respiration. Owing to the variable line of reflection of the left costal pleura over the cardiac region, a distinction between pericardial and extrapericardial friction cannot always be safely made from its situation alone, but in general it may be said that pleuro-pericardial friction is uncommon over the superficial cardiac dulness, and is usually heard outside of this region. It is influenced more than pericardial friction by the respiratory movements. If the patient stops breathing, the friction sound may diminish or disappear.

**Pseudo-pleural Intrapulmonary Sounds.**—Loud sonorous rales may occasionally simulate pleural friction. Their less jerky character and disappearance after cough may suggest their pulmonary origin.

**Pleural Crepitation.**—At times with symptoms of pleuritis, fine, medium, or coarse crackling rales are heard over the site of the suspected process. These may be pleural in origin, but can hardly be differentiated from intrapulmonary rales. Galvagni[1] finds that pulmonary rales may be transmitted to the mouth and are audible on auscultation, while pleural rales cannot be heard there.

**Blood.—White Cells.**—Fibrinous pleuritis is more often accompanied by leukocytosis than serofibrinous pleuritis. Thus, of 48 cases of primary fibrinous pleuritis, the white count was 12,000 or over in 19 (39.5 per cent.). Of these 19 cases, the white cells numbered 12,000 to 13,000 in 3; from 13,000 to 14,000 in 4; 14,000 to 15,000 in 4; 15,000 to 16,000 in 2; 16,000 to 20,000 in 3, and 20,000 to 24,000 in 3. The difference between the white count in primary fibrinous and that in primary tuberculous serofibrinous pleuritis is quite striking in the writer's small series of cases, only 3 of 33 cases in the latter group showing 12,000 or more white cells.

**Sequelæ.**—Of 345 cases in the writer's series pleural fluid was discovered as a sequence of the process in 5.

**Diagnosis.**—This is usually easily made from the presence of the friction rub. Cases with an acute onset, with cough and stitch in the side, aggra-

[1] *Riforma Medica*, 1905, No. 33.

vated by respiration, are due to pleuritis in a large proportion of the cases, even if no friction rub can be heard. The diagnosis of diaphragmatic pleurisy is often troublesome and may remain in doubt for several days. Cases in which pain along the lower thoracic margin is the only symptom are most difficult of diagnosis. To judge from the remarkable frequency with which there is postmortem indication of previous disease of the pleura, it is probable that an undetected pleurisy is the cause in a large proportion of the cases. Rarely the pain is the precursor of herpes zoster. The possibility of spinal disease must be borne in mind. Tertiary syphilis and tumor are to be considered. Lead poisoning, caries of the ribs, periostitis, and thoracic aneurism should be excluded. The *x*-rays may help in the diagnosis. Although the possibility of pleurodynia or intercostal neuralgia cannot be excluded, this diagnosis amounts to a confession of ignorance concerning the cause of the process.

In typical cases there is little danger of confusion, but the signs may be those of thickened pleura: dulness, diminished vesicular breathing, with preservation of the fremitus, even a friction rub, and yet fluid may be present. The fluid may exist between lung and diaphragm, where small amounts of fluid are likely to collect first, and may rise little above the pulmonary margin between lung and chest wall. In other cases there may be evidence of thickened pleura and oftenest in the lower anterior aspect of the chest, with fluid in the posterior inferior thoracic region. Again, fluid may be encapsulated and fibrinous pleuritis with friction co-exist. In doubtful cases an exploratory puncture must be made. Cases with complicating pulmonary disease are likely to cause most difficulty in diagnosis.

**Prognosis.**—The immediate outlook in fibrinous pleuritis is good. The more remote prospects are less favorable. Of 82 cases of primary dry pleurisy in the writer's series, 60 have been followed since their discharge from the hospital. Of these, 7 (11.6 per cent.) died within four years of pulmonary tuberculosis, one died of an uncertain cause, a second of ruptured aneurism, another of cardiac disease, and the last patient by accident. By the most unfavorable interpretation, including the patient, the cause of whose death is uncertain, 8 (13.3 per cent.) have succumbed to tuberculosis. Of the remaining 48 patients, 40 are well, or practically well, including 2 who have had hæmoptysis. The remaining 8, of whom there are 5 with hæmoptysis, have pulmonary symptoms of varying severity. Including the 8 fatal and 10 cases with hæmoptysis or pulmonary symptoms or both, 18 (30 per cent.), certainly or probably, developed tuberculosis. The patients have been followed from one to twelve years, the average interval being four to five years. The outcome of primary dry pleuritis is thus nearly or quite as bad as that of primary serofibrinous effusion. The prognosis of the secondary form is that of the underlying cause. Pain may persist after the attack; 15 patients (25 per cent.) complain of occasional or persistent pain.

**Treatment.**—The immediate indication is the relief of pain, on which the cough and dyspnœa largely depend. Rest is the first consideration. In all cases in which there is fever or severe pain, the patient should be in bed. Even in mild attacks, rest shortens the duration and may prevent extension or the occurrence of an effusion.

Fixation of the side limits the play of the pulmonary against the parietal pleura and may produce immediate relief. It may be accomplished with

adhesive plaster, of which zinc oxide plaster is best. One end of a strip of well-warmed adhesive plaster, the width of the hand and long enough to reach from the spine to the sternum, is applied against the paravertebral region. The operator then forcibly wraps the strip about the lower thoracic region so that it lies stretched over the lower ribs, and thus limits their excursion. In women with pendulous breasts, several narrow strips of plaster, extending from the paravertebral region downward and forward, from the sternum downward and backward and intersecting in the axillary region, may be more comfortable. The plaster should not be allowed to remain longer than a week to ten days, and care should be taken in its removal not to cause abrasion of the skin. A tight thoracic swathe, with shoulder and peroneal straps, has the advantage of ready removal for physical examination, and does not lead to irritation or infection of the skin. It is to be preferred for patients in bed. In some cases, perhaps from diaphragmatic involvement, fixation of the thorax fails to give relief. In such cases an ice-bag or hot-water bottle may be efficient. If these means fail, a hypodermic injection of morphine may be given. In long-standing and intractable cases Stinzing advises a trial of antisyphilitic treatment, and refers to a number of instances in which cure has resulted. Potassium iodide is especially valuable, in his judgment.

A possible source of infection should be sought, and if found in any part of the body, should receive appropriate treatment. The occurrence of dry pleuritis should always suggest the possibility of tuberculosis. The chance of this is much increased by a family history of the disease or opportunity for contagion. Careful examination of the lungs, the sputum, and the use of tuberculin may furnish positive or sufficiently suggestive evidence to justify the most rigorous treatment.

Respiratory exercises are to be advised after recovery. Oversight of the patient should not cease with the subsidence of symptoms. General measures against tuberculosis should be instituted.

## Acute Serofibrinous Pleuritis.

**Etiology.**—Serofibrinous effusions arising from inflammation of the pleural sac may be divided into three principal groups: (1) *Tuberculous pleuritis* comprises the largest and most important division. (2) *Infectious (non-tuberculous) pleuritis* stands next in frequency and is a well-defined class. (3) *Other causes* are relatively infrequent and often difficult to group. They are the product of more than one factor, such as general hydræmia or venous stasis, on which an inflammatory process is superimposed.

1. **Tuberculous Pleuritis.**—It is remarkable in how many cases serofibrinous pleuritis is apparently primary without evidence of disease in other organs. Thus of 1185 cases in the writer's series the disease of the pleura was unassociated with positive findings elsewhere in 750 (63.4 per cent.). The pleural disease was combined with suggestive or positive evidence of pulmonary tuberculosis in some part of the body in 160 (13.5 per cent.). The lung was the most frequent site of tuberculosis in this group with 149 cases, of which 47 showed tubercle bacilli in the sputum. Tuberculous peritonitis was present in 9 and tuberculosis in other regions in 2 patients.

There is good reason to believe that a large proportion of cases of sero-

fibrinous effusion, more especially the primary cases and those secondary to pulmonary tuberculous lesions, are due to tuberculosis. This point of view is largely the result of recent investigations and is based on the following:

(*a*) *Tuberculosis of Other Organs.*—In Osler's 195 cases, 30 showed tubercle bacilli in the sputum. As a symptom of pulmonary tuberculosis pleural effusion usually comes early if at all. Dense pleural adhesions commonly obliterate parts or the whole of the pleural sac in an advanced stage of the disease.

(*b*) *The Subsequent History.*—Thus, of Cabot's 152 cases of idiopathic effusion from the Massachusetts General Hospital, 15 per cent. sooner or later developed demonstrable tuberculosis of lung or bone. Of 88 cases in Osler's wards, 30 (34 per cent.) later became tuberculous. In Bowditch's 90 cases, under observation from 1849 to 1879, 32 (35.5 per cent.) died of or had phthisis. Sokolowski followed 28 primary cases for six years. In 10 (35.7 per cent.) tuberculosis developed. A series of 130 cases, with primary pleuritis with effusion, is reported by Hedges and followed for seven years. Of these, 40 per cent. became tuberculous.

(*c*) *Postmortem Evidence.*—Of 131 cases of different types of pleuritis examined postmortem by Osler, 32 were found to be definitely tuberculous.

(*d*) *The Tuberculin Reaction.*—This is positive in a large proportion of the cases—in 73.7 per cent. of Beck's series and in 7 of 8 cases by F. W. White. In the writer's series (M. G. H.) tuberculin was given in 47; 36 (76.5 per cent.) gave a positive reaction. A positive result merely means tuberculosis somewhere, not necessarily in the pleura.

(*e*) *The Character of the Exudate.*—The evidence is based on the character of the cells, the demonstration of tubercle bacilli in the fluid, and the results of animal inoculation.

*Character of the Cells.*—Lymphocytes predominate in a large proportion of serofibrinous fluids from patients known to have tuberculosis of the pleura; they are likewise in excess in cases in which pulmonary tuberculosis is certainly or probably present, and the same cellular formula is present in idiopathic pleurisy with effusion. Excess of lymphocytes is not invariably proof of a tuberculous pleurisy.

*Tubercle Bacillus in the Fluid.*—The effort to cultivate tubercle bacilli from serous effusions practically always fails. Simple microscopic examination likewise is usually unsuccessful. Of 415 cases collected by Netter from various sources, bacilli were found in only 9 (about 2 per cent.). Inoscopy or sedimentation has given more positive results. In primary cases, Jousset claimed by means of inoscopy to have found tubercle bacilli in 23 cases (100 per cent.), but other observers have failed to confirm his results, and they cannot be accepted without question. In 115 cases at the Massachusetts General Hospital in which tubercle bacilli were sought in the fluid, they were found in 24 (20.8 per cent.). Körmöczi and Jassniger[1] found bacilli in 3 of 8 cases. Zebrowski,[2] by simple sedimentation of a large quantity of fluid, prevented from coagulation by the addition of sodium fluoride, found bacilli in 12 (55 per cent.) of 22 primary cases and in 10 (83 per cent.) of 12 secondary effusions.

*Animal Inoculation.*—The most convincing proof rests on animal inoculation, the results of which are practically conclusive. Of 66 cases in the

[1] *Deut. med. Woch.*, 1904, p. 342.

[2] *Ibid.*, 1905, No. 36.

writer's series, the results were positive in 15 (22.7 per cent.). Much more striking success is obtained by using large quantities of fluid for injection. Eichhorst, with 15 cc., demonstrated tuberculosis in more than 62 per cent. Le Damany has been most successful, and his use of large amounts of fluid, from 10 to 50 and sometimes as much as 300 cc., led to positive results in all but 8 of 55 cases, while in 4 of the 8 negative cases coincident lesions indicated their tuberculous origin.

By the presence of tubercle bacilli in the sputum, in the fluid by animal inoculation or inoscopy, or by operation, Musgrave proved the tuberculous character of 28 (54.9 per cent.) of 51 primary or secondary effusions.

There can be no doubt from these considerations that tuberculosis occupies first place in the etiology of pleural effusions in any large series of cases. When such cases are demonstrated as tuberculous, it is probable that they have been so from their inception, and not through secondary infection with the tubercle bacillus, although such an event cannot be excluded as a rare occurrence. All serofibrinous effusions cannot be classed as tuberculous.

2. **Infectious (Non-tuberculous) Pleuritis.**—Infection of the pleura with other organisms than the tubercle bacillus is capable of causing serofibrinous effusion. The pneumococcus is the most frequent cause in this group. The streptococcus and other organisms may likewise be a cause. A difficulty lies in the exclusion of the tubercle bacillus as a mixed infection.

(*a*) *Metapneumonic Pleuritis.*—This appears to be a well-defined group and is represented by 62 (5.2 per cent.) of 1185 cases with serofibrinous effusion in this series.

Small effusions of a serofibrinous or purulent character are common in lobar pneumonia. Maragliano demonstrated serofibrinous or purulent effusion in 38 of 58 cases, by means of exploratory puncture. If small amounts of effusion are included, a serofibrinous is probably more common than a purulent exudate. Norris (see Pneumonia), in 127 autopsies in pneumonia, found serous in 5 and purulent fluid in 20 cases, while Kerr in 173 autopsies found 38 with serofibrinous and 6 with purulent effusion. Of 154 autopsies on cases with lobar pneumonia (M. G. H.), a pleural effusion was present in 57, and in these the fluid was cloudy in 30, clear in 10, purulent in 9, and hemorrhagic in 6. The largest amount at autopsy was 500 cc., and was unrecognized during life. The cloudiness so commonly seen in such effusions is usually due to fine fibrinous flocculi. Tuberculosis was present in the lungs or bronchial glands in 9 of the cases, in 6 of which it appeared to be obsolete, while in 1 it was a probable cause of the effusion. In Sello's cases the effusion was demonstrated at the beginning of the pneumonia in 2, during the course of the disease in 31, and afterward in 24. The independent existence of serofibrinous effusion accompanying pneumonia and due to infection with other organisms than the tubercle bacillus cannot be doubted. In support of this is its association with an inflammatory disease of the lung, usually due to the pneumococcus, the presence in the fluid of pneumococci or other organisms which alone are capable of causing pleuritis with effusion, and the absence in cases with serofibrinous effusion and pneumonia of tuberculous lesions at autopsy.

(*b*) *Rheumatism.*—This was coincident with pleuritis with effusion in 13 cases (0.9 per cent.). There is no proof that the rheumatic poison can alone infect the pleura, and it seems to the writer misleading to speak of a rheumatic pleuritis in the sense in which this term is sometimes used to designate

a pleuritis with or without arthritic symptoms, in which a favorable result is obtained following the administration of salicylic acid preparations. Until proof can be offered that rheumatism is due to a specific organism, and this can be demonstrated in pleural effusions as a cause, it is better for clinical purposes to regard only such effusions as complicate arthritis as possibly rheumatic in origin. Infection of the joints and the pleura, with discovery of streptococci in both, was associated with panophthalmitis in one case; in another the joints, the pleura, the endo- and pericardium were simultaneously involved. In both cases the pleural fluid showed an excess of polynuclear cells, viz., 95 per cent. and 65 per cent., respectively. As in other forms of pleuritis, tuberculosis must be excluded.

(*c*) *Trauma.*—Serofibrinous effusion followed trauma in 10 cases (0.8 per cent.) in this series. The effusion may be due to simple infection or to tuberculosis. Traumatic serous pleuritis has been followed by the development of pulmonary tuberculosis (Lebert), and tubercle bacilli have been found in the fluid by Chauffard, Herbert, Barjon and Lesier, and Chevastelon (quoted from Chevastelon).

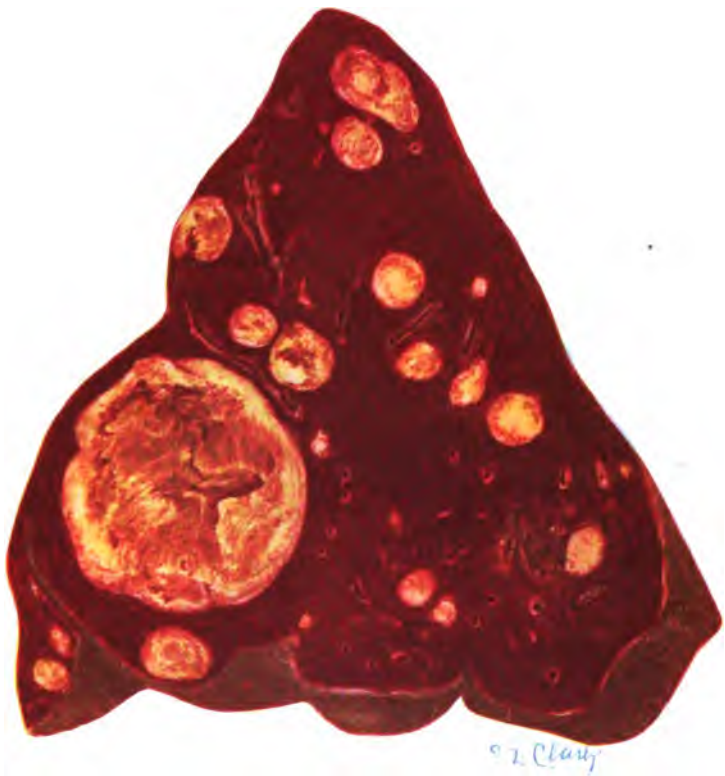
(*d*) *Typhoid Fever.*—The association of serofibrinous effusion and typhoid is rare, occurring in only 7 cases (0.5 per cent.) in this series. Among 1500 cases of typhoid, McCrae (see Typhoid Fever) noted only 3 with serous effusion. The bacilli have been obtained in pure culture from the fluid by Fernet, Achard and Gordinier, and Lartigau. In Achard's case the fluid was turbid and its agglutinative power was ten times that of the patient's blood serum. In Gordinier and Lartigau's case the fluid was greenish yellow and opalescent. Pleural effusions in the course of typhoid fever may also be hemorrhagic, but are most commonly purulent. The complication may occur early, as in Fernet's case, but is more often found during the course of the disease. It is not certain that the typhoid bacillus alone is capable of causing serofibrinous effusion. General infection with typhoid bacilli is so common in typhoid fever that the mere presence of typhoid bacilli in the exudate does not suffice to establish the independence of typhoid pleuritis. The agency of other organisms, and especially the tubercle bacillus, must be rigorously excluded. In Achard's case 20 cc. failed to produce tuberculosis in an inoculated animal.

(*e*) *Infection in any part of the body* may be a cause of serofibrinous pleuritis, although the effusion accompanying septic processes is more often purulent in character or becomes so after passing through a serofibrinous stage. Pulmonary infection resulting in bronchopneumonia, pulmonary infarction, pericarditis, malignant endocarditis, uterine sepsis, etc., may lead to serofibrinous pleuritis. In such cases the serous rather than the purulent character of the effusion may be due to diminished virulence of the infecting organisms or to increased resistance on the part of the patient.

3. **Other Causes.**—A sharp, dividing line cannot always be drawn between transudates and exudates. The presence of fibrinous flocculi or clot justifies an inclusion in the class of serofibrinous fluids. Fibrinogen is present in all fluids and an admixture with blood may cause clotting. An inflammatory process may readily be superadded to a transudate and thus complicate the differentiation.

**Special Pathology.**—1. **Pleura.**—The appearance of the pleura does not usually differ from that in simple fibrinous pleuritis. The fluid commonly occupies the most inferior parts of the cavity, and in acute cases the fibrinous

PLATE IV



Secondary Sarcoma of Lung.

layers on the two pleuræ are usually easily separated where they lie together above the fluid. Bands of adhesions may at times be found traversing the fluid and connecting the visceral and parietal layers. In the more chronic cases the two pleuræ may be more or less firmly united above the fluid. It is less common, however, to observe encapsulation of serofibrinous than of purulent fluid. Sacculated exudates, when they occur, are most common at the posterior and inferior aspect of the pleural sac. Rarely more than one encapsulation occurs, and the contents of the two may vary, in one serous, in the other purulent fluid. Miliary tubercles may occur in the pleura without fluid or fibrinous exudate. Both fluid and fibrinous exudate, however, are more common. In the gross appearance the pleura may not differ from that seen in the simple form, and tubercles may be discovered only on microscopic examination.

2. **Side Affected.**—The left side is the more frequent site of the process. Of 1085 clinical cases in the writer's series investigated on this point the effusion was confined to the left side in 570, to the right in 487, while both were involved in 28. In one case the effusion was sacculated on the left, posteriorly, near the spinal column, over an area eight inches in diameter.

3. **The Effusion.**—This is quite variable in its character. It may be largely serous, with only a small amount of scattered fibrinous flocculi. The fibrin may exist as wavy, skein-like masses in suspension, or as more compact, whitish, coarse, membranous shreds or curd-like deposits. A clot usually forms in a variable but short period after evacuation, and may be found as a small, jelly-like mass at the bottom, or may comprise almost the whole volume of the fluid, with only a thin layer of clear serum about it. The fluid is usually amber colored, with an admixture of greenish or reddish from the presence of blood. It may be brownish on removal or turn so after standing. When mixed with considerable amounts of blood it may be blood red, and, if removed after having long remained in the chest, may be darker, even chocolate colored. Most fluids are clear or only slightly opalescent from the presence of albumin, fibrin, clot, or cellular elements, which on standing tend to settle and thus clear the supernatant fluid. No sharp dividing line can be drawn between serofibrinous fluids cloudy from the presence of numerous cells and those with more or less frank admixture of pus. It must be remembered that cellular elements tend to sediment within as well as outside the chest, and that an abundance of polynuclear cells obtained on tapping the upper layers of a pleural fluid may be associated with a sediment of pus at the bottom.

(*a*) The *amount* of fluid is very variable. In cases of acute fibrinous pleuritis there is practically always more than the normal amount of fluid in the pleural sac. Even when the process is confined to the upper parts of the pleura, small amounts of fluid are often found at the bases. In 500 cases in this series the amount varied from a few to 4620 cc., the largest measured amount at any one tapping. The right chest is more capacious than the left and larger amounts of fluid are likely to be present in men than in women.

(*b*) *The Reaction.*—This varies with phenolphthalein and litmus. Both exudates and transudates are acid to phenolphthalein, with inconstant differences in the degree of acidity. "Litmus usually reacts acid to exudates, acid neutral or even alkaline to transudates, this apparent discrepancy being

due to the disodium phosphate, which reacts neutral to litmus and acid to phenolphthalein" (Miller).

(*c*) *Specific Gravity.*—The determination of this is of great value in differentiating exudates from transudates. The fluid should, if necessary, stand several hours to allow the escape of air (Miller). It is surprising with what constancy inflammatory fluids have a specific gravity of 1018 or over. Exceptions are not common even in a large number of cases. Of 224 cases in the writer's series only 19 had a specific gravity below 1018. There appears to be no noteworthy difference in the specific gravity of serofibrinous fluids accompanying primary disease of the pleura, those associated with pulmonary tuberculosis, pneumonia, rheumatism, typhoid fever, or other inflammatory processes. In transudates, uncomplicated by inflammation of the pleura, the specific gravity is usually below 1018. It has been shown that the amount of salts and extractives is very nearly the same (Runeberg, Méhu, Reuss, Hoffman) in fluids of different origin. In general, salts and extractives, after the withdrawal of albumin, amount to about 1.08 per cent. in non-inflammatory fluids and to about 1.18 per cent. in inflammatory fluids. A variation in the specific gravity of pleural fluids is dependent for the most part on differences in the amount of albumin.

(*d*) *Albumin.*—This exists in the form of serum albumin, serum globulin, and fibrinogen, to which, if present in sufficient amount, is due the property of spontaneous coagulation. Inflammatory fluids contain a relatively large amount of albumin and fibrinogen. In general, exudates have a specific gravity of 1018 or higher, with 4 per cent. or more of albumin.

*Nucleo-albumin* (*Primavera and Rivalta*) may be demonstrated by the addition of a drop of the fluid to be tested to a dilute solution of acetic acid (2 drops glacial acetic to 200 cc. water). If nucleo-albumin is present, a slight turbidity is produced in the fluid. Runeberg performs the test by adding a few drops of acetic acid to the fluid to be tested. The substance, the identity of which is uncertain, is demonstrated by marked turbidity of the fluid in exudates and very slight or no change in transudates. It is somewhat soluble in an excess of acetic acid and completely soluble in alkalies.

The determination of the amount of albumin in these fluids is of some importance in judging their origin. Estimation by weight of the precipitated proteid or the total nitrogen (Kjeldahl) is too complicated for general use. Esbach's and Purdy's methods of estimating albumin in urine are only approximately accurate for pleural fluids, as is shown by comparison with the results obtained by more exact methods. Reuss has devised a formula for estimating the amount of albumin, based on the practical lack of variation in salts and extractives and the almost constant relation between the specific gravity and albumin. By his formula $A = \frac{3}{8}(S - 1000) - 2.8$, in which A = albumin and S = specific gravity, the amount of albumin may be calculated and the error amounted to as high as 0.5 per cent. in only 1 of 24 cases in which the albumin was carefully determined by weight.

(*e*) *Fat, uric acid, cholesterin, glucose, biliary acids,* and *pigments* are occasionally found.

(*f*) *Cellular Elements.*—The sediment obtained after standing or sedimentation shows red blood corpuscles, polynuclear leukocytes, small mononuclear (lymphocytes) and endothelial cells. Eosinophiles and mononuclear cells intermediate between the small lymphocyte and endothelial

cell are common, but usually comprise only a small proportion of the total number. An occasional mast-cell is not an infrequent finding.

*Tuberculous Fluids.*—During the first few days following tuberculous infection of the pleura there may be an excess of polynuclear cells, as has been shown by Widal, Tulland, Wolff, and others, but it is generally agreed that fluids due to tuberculous pleuritis show an excess of lymphocytes. In 28 cases (M. G. H.), proved to be tuberculous by the finding of tubercle bacilli in the exudate or positive inoculation, the lymphocytes numbered 90 to 100 per cent. in 24, 88 per cent. in 1, and from 70 to 75 per cent. in the remaining 3, of which 2 showed 15 per cent. endothelial cells, the third 16 per cent. eosinophiles. The lymphocytes thus predominated in all.

In effusions arising in the course of pulmonary tuberculosis, the lymphocytes have likewise been shown to predominate, but, owing to the chance of mixed infection from the lung, a variable and at times considerable proportion of polynuclear cells may be present. Of 19 cases examined by Miller, the lymphocytes comprised 95 per cent. or more in 16. Neutrophiles predominated in 1. In 28 cases with probable or certain pulmonary tuberculosis (M. G. H.) the lymphocytes numbered 80 to 100 per cent. in 20. In 6 the leukocytes were degenerated, in 1 there were about equal proportions of polynuclears, endothelial and other mononuclear cells, while in the last case the endothelial cells numbered 85 per cent.

Idiopathic effusions likewise show a predominance of lymphocytes, and for this as well as other reasons should be mentioned in this group. In 100 cases (M. G. H.) the lymphocytes ranged from 70 to 100 per cent. in 85. In 14 of the remaining cases polynuclear cells were in excess, in explanation of which a mixed infection may be suspected. Small endothelial cells reached 15 per cent. in 2, in 1 case numbering 65 per cent.

Unfortunately, not all fluids showing a predominance of lymphocytes can be regarded as tuberculous from the cellular formula alone. Miller had one case of unknown origin with 97 per cent. lymphocytes and no reaction to tuberculin. In 2 cases (M. G. H.) of idiopathic effusion, with counts of over 95 per cent. of lymphocytes, there was no reaction to tuberculin. Naunyn has observed that long-standing transudates may show an excess of lymphocytes, and this is confirmed by one of the present series with 95 per cent. lymphocytes in a fluid later shown by autopsy (M. G. H.) to be due to chronic passive congestion and not to tuberculosis. Despite the exceptions, however, a predominance of lymphocytes must be regarded as strongly suggestive of tuberculous pleuritis, especially when passive congestion can be excluded.

*Infectious (non-tuberculous) Fluids.*—Infection of the pleura with other organisms than the tubercle bacillus usually gives rise to an excess of polynuclear cells in the exudate. Musgrave studied 12 cases; the polynuclear cells predominated in all. Miller reported 7 cases. The neutrophiles were in excess in most, but in 2, one of whom failed to react to tuberculin, there were 97 per cent. of lymphocytes. In the writer's series there are counts on 16 cases. In general, the fluids differed from those obtained in tuberculous cases in their more turbid character, the lower percentage of lymphocytes and higher proportion of polynuclear and endothelial cells. In 1 of 11 metapneumonic effusions the lymphocytes numbered 82 per cent. In 2 cases associated with an arthritis, there were 65 and 95 per cent. polynuclears. The lymphocytes predominated in 2 of 3 cases in which the

effusion followed trauma. Tuberculosis could not be excluded. Naunyn states that lymphocytes may predominate in acute cases which are subsiding or in mild infections.

For transudates, endothelial cells in large numbers occurring especially in sheets or plaques, are characteristic, but lymphocytes may predominate in mechanical effusions of long standing. A secondary infection may modify the cellular formula, with relative increase in polynuclear cells.

The value of cytology in the diagnosis of the cause of pleural effusions has proved somewhat less valuable than was at first anticipated. The exceptions are too numerous to admit of definite conclusions from the cells alone, but the method is of assistance with other factors in any given case.

4. **Intrapleural Tension.**—With small effusions this may still be negative. As the fluid increases in amount the tension rises and becomes positive after the pulmonary elasticity is spent. Various factors influence the pressure. It may be relatively high with a small amount of fluid if pulmonary retraction is prevented by pleural adhesions, by pulmonary or mediastinal disease. Pitres[1] finds that the pressure may vary from 0 to + 2 or + 3 with less than 1000 cc., from + 8 to + 22 with 1000 to 2000 cc., and from + 20 to + 48 mm. Hg. with more than 2000 cc. The pressure fluctuates with the phases of respiration. An initial positive pressure may fall during deep inspiration to — 40, as noted by Schreiber.[2] After aspiration the fall may be greater and with deep inspiration even to — 90 mm. Hg. The fluid is also under a pressure of its own fluid column and the tension thus varies at different levels.

5. **Mechanical Effects of the Exudate.**—If we estimate the total air capacity of the lungs as roughly from 4000 to 6000 cc., it is obvious that the presence in one pleura of even a half of this amount must displace other organs. With small effusions the lung bears the brunt; it contracts and becomes atelectatic. With large effusions it is compressed, completely emptied of air, and for the most part of blood, and may be found as a brown mass, not larger than the closed fist, lying against the spinal column in the upper and posterior part of the affected side. In the absence of long-standing and extensive inflammatory changes it is still capable of re-expansion after removal of the fluid. Under less favorable circumstances, extensive adhesions, the formation of dense connective tissue on its surface and within its substance may prevent this. Such a result is much less common with serofibrinous than with purulent exudates, and since it has become the custom to tap early.

In consequence of diminished negative pressure within the thorax, the intercostal spaces show less than their normal depression. Early in the disease they may be narrowed from spasm of the intercostal muscles. With large effusion and increase in size of the affected side the spaces may actually be widened from pressure, and perhaps, also, from paralysis of the intercostals. Later, following the absorption or removal of fluid, the thoracic wall may be depressed, and the intercostal spaces narrowed from contraction of scar tissue. The diaphragm, and with it the liver or spleen, is at first depressed from the loss of the normal negative intrathoracic pressure. With large effusion, the diaphragm is forced downward by positive pressure from

[1] *Arch. clin. de Bordeaux*, 1896, 5, p. 70.
[2] *Deut. Arch f. klin. Med.*, 33.

above and the weight of the superimposed fluid. The dislocation of the mediastinum and the heart from small effusions is a result of a disturbance of equilibrium between the two pleural sacs. It is dislocated by positive pressure with large effusions. Pressure on the œsophagus may lead to dysphagia, and pressure on or invasion of the region about the vagus, to recurrent laryngeal paralysis.

The ultimate causes of circulatory symptoms have been the subject of much experimentation. They do not appear to be due to changes in the blood pressure from narrowing of the pulmonary circulation, which may be obstructed even to four-fifths of its extent without a permanent fall of blood pressure (Lichtheim *et al.*). Even a slight increase of intrathoracic pressure, however, leads to considerable circulatory disturbance, as is seen in the swelling of the cervical veins in coughing and straining. D. Gerhardt[1] believes this to be due to diminished outflow of blood from the intrathoracic veins, obstruction to the pulmonary capillaries and veins, and reflex depressor action. Compensation may be affected by increased depth of respiration. Toxins, fever, carbon dioxide poisoning, or existing cardiac disease may likewise be factors.

6. **Absorption.**—Various factors probably play a part in absorption. Hydræmic and congestive transudates are rapidly absorbed under favorable conditions. Inflammatory fluids containing relatively few formed elements and fibrin may likewise spontaneously disappear. Purulent fluids, however, may remain indefinitely unless evacuated by perforation or operation. Large effusions are less often absorbed. The mechanism is probably largely mechanical. Small, serous effusions, unassociated with fibrinous obstruction of pleural lymphatics, and interfering relatively little with respiratory changes of intrapleural pressure, are most favorable for absorption, while the opposite obtains in large and inflammatory fluids. West[2] refers to the "lymphatic pump," the action of which is suspended by fibrin plugging the pleural stomata and large effusions which prevent expiration on the affected side. It is probable that osmosis, also, is a factor. Rothschild[3] finds that fluids showing less molecular concentration than the blood, as indicated by a higher freezing point, are more likely to be absorbed than those in which the opposite relation obtains. In the latter instance abstraction of fluid from the blood may increase the amount of pleural fluid until isotonicity is established.

**Symptoms.**—1. **Primary Form.**—Prodromata are uncommon. Slight cough and failing health may precede the onset. An initial chill is rare; chilliness is common. The disease began gradually in more than one-half (60 per cent.) of the writer's series. There is malaise, pain of variable intensity, fever, and cough. Sudden onset, in which the patient's activity is abruptly interrupted, is less common. In exceptional cases the initial features may suggest pneumonia. There is chill, fever, and severe pain in the side, but no rusty sputum. An insidious onset, especially at the extremes of age, is not infrequent. In a small proportion the symptoms are sufficiently characteristic to suggest the diagnosis from the history of initial pain, which gradually diminishes or stops as the fluid accumulates and the dyspnœa increases. The temperature may gradually rise as long as the

[1] *Zeit. f. klin Med.*, 1904, lv.
[2] *Lancet*, March 25, 1905.
[3] *Deutsch. Aerztztg.*, 1901, Heft 40, 241.

fluid increases, is continuous during this period, intermittent with the effusion at a standstill, and often absent during absorption. It may reach normal at the end of a week or ten days, although continuous or irregular fever may last for a much longer period. The exudate may be discovered by the third or fourth day, if untapped, may gradually increase during the next ten days, then gradually diminish, to disappear in favorable cases during the third, fourth, or fifth week of the illness.

The disease is often atypical. General symptoms and fever may predominate, and, aside from the pulmonary findings, typhoid fever may be suggested. Pain in the abdomen, with muscular spasm and tenderness, may mislead the observer into the diagnosis of an acute abdominal affection. Both onset and course may be latent or sudden, severe, even rapidly fatal (pleuritis acutissima). There may be an initial chill, rapid rise of temperature, intense dyspnœa, cyanosis, rapid pulse and respiration, delirium, and death in a few days with symptoms of suffocation. An immediate resort to evacuation may be life saving in such cases.

2. **Secondary Form.**—The onset and course are often so masked by the existing disease that symptoms referable to the pleura are unnoticed or absent. The presence of pleural effusion may then be discovered only during a routine physical examination, or, if this is neglected and the disease is fatal, at autopsy. The presence or absence of symptoms largely depends on the mildness or severity of the primary disease. In pulmonary tuberculosis, however, the symptoms may be typical, since effusion usually occurs early, if at all, in its course, from the frequent obliteration of the pleural sac by adhesions in the more advanced stages. In lobar pneumonia, typical symptoms of effusion are usually lacking or only with difficulty differentiated from those due to the pneumonia itself. There may be an accession of pain, dyspnœa, or cough. The respirations, pulse, and temperature may rise above their previous level. A failure of the temperature to drop at the expected time may be the first indication.

3. **Special Symptoms.**—*Pain.*—This is usually one of the first and most typical symptoms. It was present in 89 of 100 cases of primary serofibrinous effusion in this series. It may be absent, as in 5 cases. Associated tenderness over the inflamed pleura is frequent.

*Cough.*—This is probably next in frequency, occurring in 83 per cent., absent in 12 per cent., and not given in 5 per cent. It is usually short and dry, but may be accompanied by expectoration (48 per cent.). The sputum is mucoid or muco-purulent; rarely it may contain blood (2 per cent.) Cough alone may be due to pleural irritation. Expectoration should suggest a pulmonary complication, usually an infection, more rarely œdema, evidence of which may be furnished by the character of the sputum.

*Respiration.*—Short, quick respiration is frequent in the early stages from pain and spasm of the respiratory muscles. The rate may be elevated from fever, encroachment on the thoracic space by fluid, associated pulmonary disease, or embarrassment of the circulation from pressure. The normal relation between the rate of respiration and pulse is much more often maintained with pleural effusion than with pneumonia. Quick respiration is more often observed at the onset and after exertion. When the patient is at rest and the exudate has gradually accumulated, one side of the chest may contain its full capacity of fluid without disturbance of the normal respiration-pulse ratio.

*Dyspnœa.*—The embarrassment of respiration may amount to dyspnœa. This is more frequent in rapidly formed and large accumulations, and may become orthopnœa. At times, however, with small effusions and much limitation of respiratory motion, there may be marked dyspnœa. Cyanosis, with or without turgescence of the cervical veins, is likely to accompany marked interference with respiration.

*Temperature.*—There is no typical fever curve. The temperature is more often elevated and in general reaches a higher level than with dry pleurisy. Of 100 primary cases in the writer's series, only 10 were without fever. From 100° to 102° is an average pyrexia. In rare instances the temperature may reach 104° to 105° or higher. It is likely to be high in children and robust patients. Absence of fever is occasionally observed in old or debilitated patients and in terminal infections, when it may be subnormal.

*Pulse.*—This presents no special features. The rate usually corresponds to the fever curve. The rapid accumulation of a large amount of fluid may embarrass the circulation and cause a rapid and feeble pulse.

*Febrile or Toxic Symptoms.*—These are not especially characteristic and are such as may be seen in other infectious processes. At the onset there may be headache, insomnia, malaise, and general pains. The skin is hot and dry. As the fever drops, there may be sweating, which may become a prominent symptom if the process is long continued. There may be thirst, anorexia, even nausea and vomiting, but gastric disturbances are uncommon. In protracted cases the loss of strength and weight may be marked.

*Hoarseness* may be due to pressure on or paralysis of the recurrent laryngeal nerve. *Dysphagia.* Interference with the passage of food from pressure on the œsophagus may be present. Ferber has observed that the passage of food through the œsophageal foramen may be accompanied by pain, when there is diaphragmatic pleurisy. *Singultus.* This is a rare and interesting symptom. It may be most distressing when the diaphragm is involved.

*Urine.*—During the acute stage of the disease, the urine presents the usual features common to febrile disturbances. It is small in amount, of high color and specific gravity, with an increase of urea and uric acid and a diminution in the chlorides. During absorption, the amount of urine may rise rapidly with an increase in the output of chlorides, the so-called "chlorine crisis," while urea and uric acid are diminished. Traces of albumin and a few hyaline casts may be present and can be ascribed to fever, toxæmia, or rarely to stasis.

**Physical Signs.**—Small amounts of fluid collect in the most dependent part of the thoracic cavity, in the costophrenic sinus posteriorly, and in the region between lung and diaphragm. Until the amount of fluid becomes considerable, it intervenes very little between lung and chest wall. In Garland's experiments there was scarcely a trace of a rim of fluid between the lower border of the lung and the chest wall, with injections which occupied less than one-third of the thoracic cavity. In explanation of this it is assumed that there is a greater elastic traction in the lower than in the upper parts of the lung. Larger amounts of fluid finally intervene between lung and chest wall. In favorable and uncomplicated cases, 250 cc. of fluid in an adult should not escape detection. In infants 100 cc. may be discovered.

**Inspection.**—Herpes is uncommon. Inspiratory dilatation of the alæ nasi is less frequent than with pneumonia. The position of the patient is

variable. If there is dyspnœa, the patient may be more comfortable sitting upright, from the greater mechanical advantage and from the removal of the weight of the effusion on the lung which this position affords. With small effusions, without orthopnœa, the patient may be more comfortable on the unaffected side. The explanation of this is not clear. Traube has assumed it to be due to the relief of pain from removal of pressure on sensitive nerves in the affected pleura. With large effusions, the patient usually chooses a position on the affected side, thus allowing the sound lung full play and diminishing pressure on the mediastinum. It is not uncommon, even with large effusions, to find the patient lying comfortably on the back. At times an ambulant patient presents himself with a large effusion.

In the early stages of the disease, when there is pain and only a small amount of fluid, the appearance of the thorax does not differ from that described under Fibrinous Pleuritis. With the increase in the amount of pleural fluid, there is progressively less expansion and elevation of the affected side. The presence of pain always still further limits thoracic motion. Diminished motion may often be apparent as a delay in expansion of the lower parts of the chest during the first part of inspiration. With large amounts of fluid, expansion and elevation may be absent. The intercostal spaces in spare individuals may be seen to have lost their normal depression and may even be widened and fuller than normal. An increase in size can be confirmed by the tape, even as much as an inch or an inch and a half greater than the opposite side. The skin may appear somewhat shiny and smooth from obliteration of normal furrows and depressions. Œdema of the skin and dilatation of the superficial veins may occur, but are rare with serous effusion. Weisz[1] finds that the phonation's phenomenon (visible voice vibrations) is transmitted through fluid and may separate its lower limit from the upper border of the liver.

In consequence of the fulness of the affected side, the distance between the median line and the nipple in front and the scapula behind may exceed that on the normal side. With large effusions the corresponding hypochondrium may be fuller; the shoulder and with it the outer end of the clavicle stand at a higher level. Following partial or complete absorption or withdrawal of fluid, the affected side may be somewhat diminished in size and the intercostal spaces narrowed. Slight lateral deviation of the spine may accompany this retraction. Retraction and scoliosis are much less marked after serous than after purulent fluids.

The diaphragm shadow is absent on the side of the effusion. It usually remains absent after recovery, but may return, although practically always of diminished amplitude. The position of the cardiac impulse should be inspected. Evidence of pleuro-pericardial adhesions may be obtained by systolic depression of the intercostal spaces in an abnormal position in the cardiac region.

Rarely pulsation of the chest wall may be observed with serofibrinous effusion, but is more common with pus. The pulsation may be confined to a locally bulging area; it may be circumscribed without tumor or may be diffuse. Twelve instances have been reported, among others, by Cruveilhier, Flint, Broadbent, and Osler. Four cases of pulsating hæmothorax have been observed by Vialle and Braun, Montégre, McPhedran, and Sailer,[2] who

[1] *Prag. med. Woch.*, 1905, xxx, 261.
[2] *American Journal of the Medical Sciences*, 1904.

gives an account of the literature to 1904. In Sailer's case there was true expansile pulsation of the whole thorax.

**Palpation.**—This may confirm the results of inspection. A difference in the expansion of the two sides of the chest, the condition of the intercostal spaces, the degree of separation of the ribs, the position of the cardiac impulse and pulsations in other parts of the chest may be more evident to the hand than the eye. Pulsation, indeed, may be so slight as to be appreciated only by the hand. Przewalski[1] has noted a narrowing and a more marked resistance to pressure in the interspaces. This may occur early in the disease from spasm of the intercostals, and is an important sign. The interspaces may be narrowed even when the affected side is increased in size. A friction rub may be felt before the onset of effusion; it may be palpated outside the limits of fluid during the course of the disease and may return following absorption. The temperature of the affected side is higher. Œdema and fluctuation are rare with serous effusion. The liver or spleen may be displaced downward. The diaphragm may be so far depressed as to be felt below the costal margin.

The tactile fremitus is practically always absent; it is rarely present, but usually even then diminished, in children, with adhesions between the visceral and parietal pleura, or with small effusions. This is one of the most important signs of fluid; and the dividing line between lung and fluid can often be sharply drawn at the level at which the voice vibrations are lost. The tactile fremitus above the fluid may be diminished, maintained, or increased, depending on the condition of the pleura and the lung. Unfortunately, fremitus cannot always be obtained in women or children, owing to the high pitch of the voice, or the presence of an abundant layer of subcutaneous fat. Acute or chronic inflammatory thickening of the pleura diminishes, although it practically never abolishes, the fremitus. In the performance of thoracentesis a localized area where fremitus is maintained should not be chosen because of the possibility of pleural adhesions at this place.

**Percussion.**—Light percussion is far superior to heavy percussion in bringing out slight changes in the pleura. Early in the disease, when there is only a small amount of fluid, no change in the percussion note may be detected. As the fluid increases in amount, there is dulness at the base. As the fluid rises, the note becomes less resonant and finally flat. The region of flatness and absent tactile fremitus correspond. The quality of the percussion note over effusions of considerable size is usually very suggestive. It is of short duration, lacking in volume, of high pitch, very nearly like the note obtained on percussing the thigh. It is very difficult to mark on the chest the exact upper limit of fluid. With considerable fluid, three zones with well-marked differences in the percussion note can be made out in the anterior and more often in the posterior thoracic regions. Normal or diminished vesicular resonance may be obtained in the uppermost parts of the chest. Between this region and the fluid the note is dull, but has a tympanitic quality (Skoda's resonance), due to retraction or compression of the lung and vibration of air in the bronchi or trachea. Below, there is flatness from fluid. The intermediate dull or dull and tympanitic area is usually most marked behind in the interscapular region, but with large effusions may be detected in front under the clavicle. If an

[1] *Cent. f. Chir.*, 1902, xxix, p. 377.

arbitrary distinction be made between resonance and dulness and dulness and flatness, a triangular area of dulness or dull tympany can be marked out in the interscapular region, between the relatively normal lung above and the fluid below. This triangle has for its base the vertebral column, for its lower side the lower limit of lung, corresponding to the beginning of flatness, for its upper limit the beginning of dulness. The triangle represents the retracted or compressed lung, which may be apposed to the chest wall in this region. Its recognition is important for the correct determination of the upper limit of the effusion. The tympanitic note observed above the layer of fluid, as over pulmonary cavities, may change in pitch with the mouth open and closed (Williams' tracheal tone) during inspiration and expiration (Friedreich's phenomenon), and on changing the position of the patient (Gerhardt's phenomenon). A cracked-pot sound also may be heard in the absence of cavity.

With right-sided effusion, the dulness merges below with that of the liver. On the left, the tympany from inflation of the stomach with gas may be confusing and mask slight changes in the note from fluid. With considerable fluid in the left pleura, the normal tympany of the semilunar space between liver and spleen (Traube's semilunar space) may be obliterated.

*Curved Line of Flatness in Pleural Effusions.*—The limitation of fluid by dulness by some observers and flatness by others is responsible for much confusion in the description of the line assumed by the upper border of pleural fluid. If the dull triangle mentioned above be included, the upper limit of fluid is nearly horizontal behind. With a small or medium effusion, however, the line of flatness only should be regarded as indicating its upper limit.

Damoiseau was the first to note that the upper limit of flatness was a curved and not a straight line. Ellis, of Boston, correctly traced the curve, which Garland[1] verified clinically and explained by a series of experiments.

For the demonstration of the curve the patient must be in the upright position. It is best indicated by light percussion, in parallel lines, perpendicular to the upper line of the effusion, which, in general, is transverse about the chest. With small or medium effusions, the general shape of the curve is that of an elongated "S,' lowest behind, advancing upward and forward to the axillary region, where it is highest, thence to slope gradually downward. With large effusions the curve may be flattened out to assume a more nearly horizontal line. The curves of the line of flatness correspond to the line of apposition between the lower border of the lung and the pleural fluid. It is thus the shape of the lower border of the lung which gives to the line the shape of the elongated letter "S." The elastic retraction of the lung supports a certain volume of fluid and prevents its upper limit from assuming a hydrostatic level.

The curve may be of diagnostic value as a confirmatory sign of pleural effusion. It cannot be demonstrated in circumscribed effusions, in the presence of adhesions, or in other than the upright position. Pulmonary infiltration, by diminishing the elasticity of the lung, may render difficult or prevent the demonstration of the curve. It makes no difference whether

[1] *Boston Medical and Surgical Journal*, September 17, 1874, and *Pneumono-Dynamics*, Boston, 1878.

the fluid be serum or pus. The curve is more pronounced with fluids undergoing absorption or after partial removal by tapping, a possible explanation for which may be the presence of pleural adhesions in the lateral thoracic region, maintaining the lung at a higher level here, while posteriorly, where fluid collects in greater amount, its intervention between lung and chest wall may prevent the formation of adhesions.

*Shifting Dulness.*—An important feature of the dulness due to pleural effusion is its change on changing the position of the patient. This is especially true of small and recent effusions. With the patient upright, then in the horizontal position, the upper border of fluid changes its level. It is absent in the presence of encapsulating adhesions and may be slight or absent with large effusions. Due allowance in noting shifting dulness must be made for normal changes in the percussion note over the chest in different positions. The posterior inferior parts of the lung, where the test is usually made, normally become more resonant when the patient assumes a horizontal position, as in bending forward or lying face downward. The maintenance of one position during the development of an effusion is capable, to a certain extent, of modifying the location of the fluid. If the patient has been constantly on his back, the upper limit of fluid is likely to be higher behind, and small effusions may be confined to the back and the posterior axilla. It should be remembered in testing shifting dulness that the fluid may change its position only slowly.

*Sense of Resistance.*—In addition to the lack of resonance or other peculiarities of the percussion note appreciated by the ear, the lack of vibration and sense of resistance may be apparent to the finger as well.

**Auscultation.**—Early in the disease, a friction rub may be heard. Its presence does not exclude fluid, which may exist between lung and diaphragm or in the neighborhood of apposed pleural surfaces. With small effusions, the rub not infrequently persists in the lower anterior or lateral portions of the chest. The disappearance of this sign as fluid accumulates is probably due not so much to intervention of fluid between lung and chest wall as to the mechanical obstruction to the expansion of the lung. The re-appearance of friction in cases with pleural effusion is favorable, indicating diminution or disappearance of the fluid, provided extension of fibrinous pleuritis to previously uninvolved parts be excepted.

Crepitation, resembling that in the early stage of lobar pneumonia, and audible at the base of the lung, may also be heard in cases which later develop demonstrable fluid. Its explanation is not quite clear. It may be ascribed to fine pleural friction, to air entering fluid in alveoli underlying an inflamed pleura, and to expansion, during inspiration, of a slightly retracted and atelectatic lung, giving rise to crepitation coincident with the separation of previously apposed alveolar walls. A similar sound may also be heard at the termination of the disease, and may indicate that the pleural layers are again approximated, or that air is again admitted to the base of the lung.

*Breath Sounds.*—Changes in the breath sounds in uncomplicated pleural effusion are due to several factors, more than one of which usually operate in any given case. They depend on diminished expansion of the lung, from spasm or paralysis of the respiratory muscles, to changes in the lung itself from retraction or pressure, and to the presence in the pleural cavity of fluid which modifies or may even abolish the vibrations conducted from the lung to the chest wall.

Early in the course of the disease irritation of the pleura and pain diminish the respiratory murmur from spasm of the respiratory muscles and fixation of the side. Even slight exudation without pain may do likewise from the mechanical obstruction of fluid. In the presence of fluid, however, the retraction and increased density of the lung may give rise not only to a diminution in the intensity of the respiration, but to a change in its character. With small effusions, the inspiration is merely diminished, while expiration is abnormally long, somewhat higher pitched, and slightly bronchial in character. As the fluid increases in amount, the breathing over the base of the lung may have a distinctly tubular quality. This is often most marked in the interscapular region above the level of the fluid. With large effusions the breathing is vesicular in the upper part of the chest; it may be bronchial above and absent below the level of the fluid. When the lung is completely retracted and compressed, there may be almost no respiratory murmur over the affected side. At times the breathing may have an amphoric character in the upper part of the chest. Rales, as well as bronchial breathing, may have a metallic quality and thus suggest cavity. In children the breathing is more likely to be bronchial than in adults. With the subsidence of the effusion the vesicular breathing returns, but may for long or even permanently remain somewhat diminished. As the atelectatic lung expands, rales can usually be heard. An accompanying catarrh or œdema of the lungs may give rise to rales on the side of the effusion which may have a consonating quality from pulmonary compression. The breathing over the unaffected lung is often increased with prolongation of expiration.

*Voice Sounds.*—The voice sounds are often increased above, diminished or absent below the level of the fluid. The voice may have a peculiar nasal or bleating quality, the so-called œgophony. It must be admitted that the sound has only a remote resemblance to the bleating of a goat, but there is often an indescribable and very suggestive character to the vocal resonance. It is most often heard in the posterior and lower thoracic regions. The whisper is variable, but in general is increased over the region where bronchophony is heard, and may have a bronchial character. It is usually diminished or absent over the fluid. It is said by Bacelli to be transmitted through a serous and not through a purulent exudate, but the sign is not reliable.

**Examination of the Heart.**—Dislocation of the heart is one of the most important signs of pleural effusion. The position of the visible impulse should be noted. It may be seen to either side of the sternum. If the apex is behind the sternum, there may be no visible pulsation. At times an impulse is seen below the ensiform in the upper epigastric region. Palpation for the systolic impulse in the spaces on either side of the sternum may furnish more definite information. In some cases pulsation can be neither seen nor felt, and reliance must be placed on auscultation. Greene[1] finds that rhythmic lateral displacement of the heart is a valuable sign of unilateral pleural fluid. It may be demonstrated by inspection, auscultatory percussion, or the fluoroscope. A systolic murmur is not infrequently heard over the displaced heart, and is probably due to pressure on the great vessels, especially the pulmonary artery.

[1] *American Journal of the Medical Sciences*, 1906.

**Special Physical Signs.**—1. **Displacement of the Heart.**—(*a*) *Away from the Affected Side.*—An accumulation of air, fluid, or other foreign material in one pleural sac allows the lung on that side to contract, and thus exhausts a part of its elastic force. The intrapleural tension on the affected side is correspondingly increased, while that on the unaffected side is still maintained at or nearly at its former level. The mediastinum is thus subjected on either side to unequal pressure, and seeks a position of equilibrium between the two. Because of the firmness with which the mediastinum as a whole is held in place by ligamentous bands and bloodvessels branching in various directions, its displacement is less marked than that part of it occupied by the heart, which is attached above to the relatively immobile aorta, but is elsewhere capable of considerable lateral motion within the elastic parietal pericardium. It seems more in accordance with the mechanical factors involved to regard cardiac displacement as due to a thrust or "push" of the relatively higher intrapleural pressure in the diseased sac than a "pull" from the relatively lower pressure in the normal side.

Provided the heart is free to move laterally, its displacement may be one of the first signs of an accumulation in the pleural sac. As shown by Powell, the intrapleural pressure on the diseased side need not be actually positive. Apposition of fluid or other material with the heart is not a necessary factor. Because of the normal position of the heart to the left, it is always displaced a greater distance to the right with left-sided pleural disease than to the left with disease of the right pleura. To judge from Carrière's observations and experiments, the amount of fluid in the left chest may reach 700 cc. without displacement of the heart. The writer has seen slight cardiac displacement develop under observation in a girl of fourteen, from whose left pleura 250 cc. of pus were evacuated by operation. Cardiac dislocation may be noted before dilatation of the side is evident, as was pointed out by Houghton in 1834. As much as 1000 cc. of fluid may be present in the right pleura without evident displacement of the heart to the left. In such diseases as pneumonia, in which pleural fluid may occur as a complication, or in cases in which its presence is suspected, a careful record of the position of the heart may be of unexpected value later in the course of the disease, when a slight deviation from its originally recorded position may be a deciding factor in a diagnosis, otherwise doubtful because of pulmonary changes complicating the physical signs. Since cardiac displacement depends not only on a loss of retractile force in the lung on the diseased side, but also on the maintenance of elastic tension in the opposite lung, any interference with the latter from disease will correspondingly limit the cardiac excursion toward that side. Thus pleural adhesions, pneumonic infiltration, emphysema, or other structural changes may so diminish the elastic power of the uncontracted lung as to limit or even prevent cardiac displacement.

(*b*) *Toward the Affected Side.*—Occasionally in the course of long continued pleural disease, absorption may lead to an increase of negative pressure on the diseased side. The heart may then be pushed toward this side by the relatively greater but still negative pressure in the unaffected pleura. Thus far mention has been made only of cardiac displacements from differences of intrapleural pressure. The heart may, however, actually be pulled to one side by the contraction of adhesions between it and neighboring structures.

(c) *Position of the Displaced Heart.*—The studies of Powell, Ferber, Bard, Pitres, and others show that in the displacement to the right with left-sided effusions the heart practically always maintains its position with the apex to the left of the base, pulsation to the right of the sternum arising at the base of the heart. In Lafforgue's[1] case, however, with a large effusion of blood in the left pleural sac, the heart was found at autopsy pointing to the right.

2. **Diaphragm Phenomenon.**—Gerhardt[2] referred to this, but thought it of rare occurrence and limited, for the most part, to emaciated individuals. Litten[3] observed its presence in all normal individuals, more accurately described its clinical appearance, and emphasized its importance in pathological conditions. He found it represented in Michael Angelo's figure of the dying Adonis in the court of the Bargello at Florence.

With the patient and the observer correctly placed, one may see in practically all normal individuals a transverse shadow descending with inspiration and ascending with expiration over a narrow zone in the lower anterior and lateral regions of the chest. It begins above in the region of the seventh rib, intersecting the ribs at an acute angle as it descends on deepest inspiration a distance of two to three spaces, or about 6 to 7 cm., to ascend to its original position with expiration. On superficial respiration, its amplitude is about one to one and a half spaces. It is best seen between the axillary and mammary lines, but may be followed through the axilla and the back, with the patient lying on the abdomen. It is highest in front, descends somewhat toward the axilla, then runs in a nearly horizontal line toward the spine, and is lost between the angle of the scapula and the spinal column. During inspiration, the differences of pressure in the thorax and abdomen are expressed on the thoracic wall as a horizontal furrow. A short interval elapses between the beginning of inspiration and the appearance of the phenomenon.

The sign is of value in unilateral pulmonary or pleural disease. It is absent in pneumonia of the lower lobes, is diminished in amplitude or absent and abnormally low in the presence of pleural fluid or air. The excursion is diminished, distorted, or irregular in the presence of pulmonary infiltration (as in tuberculosis), thoracic retraction, following pleural or pulmonary disease, pulmonary or pleural tumors, and with pleural adhesions. With enlargement of the liver or spleen, with abdominal fluid or tympanites, it may be diminished in amplitude and abnormally high. The sign may be of assistance in the diagnosis of subphrenic abscess, simulating suppuration in the lower thoracic region. The presence of the shadow above the involved area, although of diminished amplitude, may definitely indicate the subdiaphragmatic site of the lesion. It is also of value in distinguishing pneumothorax from diaphragmatic hernia, being absent in the former, but present in the latter.

3. **Paravertebral Triangle of Dulness.**—The presence of a normal triangle of dulness at either side of the spinal column in the inferior thoracic region makes the pathological triangle more difficult of interpretation and somewhat limits its value as a diagnostic sign. On percussion of the spinal column from above downward, the note becomes progressively duller as its lower

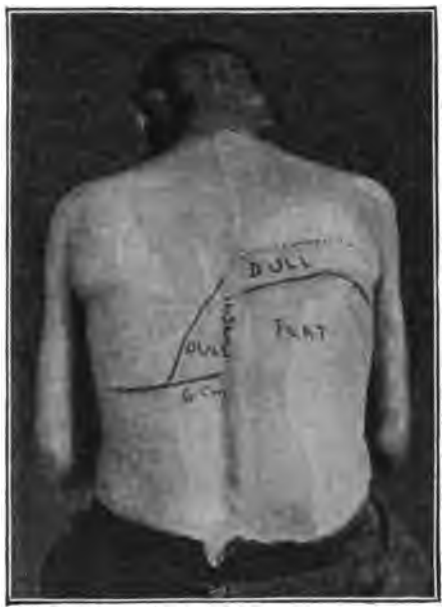
[1] *Gaz. des hôp.*, 1902.
[2] *Der Stand der Diaphragmas*, Tübingen, 1860.
[3] *Deut. med. Woch.*, 1892, and *Verhandl. d. Cong. f. inn. Med.*, 1895.

thoracic limit is approached. The degree of normal dulness in this region can be appreciated only by experience.

Korányi's[1] and Grocco's observations on this sign have since been confirmed by many observers. Specially noteworthy are the observations of Baduel and Siciliano[2] on its explanation and the series of clinical cases studied by Thayer and Fabyan.[3]

Having determined the limits of a suspected effusion by percussion and similarly outlined the lowest limit of pulmonary resonance on the unaffected side, the spinous processes of the vertebræ are percussed from above downward and the point noted where relative dulness begins. This usually corresponds to the level of relative dulness on the affected side, and somewhat higher than the level of flatness. Percussion of the unaffected lung in horizontal lines toward the spinal column discloses a paravertebral area of relative dulness of a triangular shape. The vertical side of the triangle coincides with a line drawn through the spinous processes of the vertebræ, the base with the limit of pulmonary resonance on the sound side. Its outer side is formed by a line extending obliquely downward and outward. The height of the vertical and the width of the base line vary with the size of the effusion. The base may thus vary from 2 to 7 cm. in length. The triangle is somewhat larger in right-sided effusions. It may differ from the normal triangle only in the degree of dulness. In Thayer and Fabyan's series a small but distinct triangle was detected with a left-sided effusion, which on tapping disclosed only 250 cc. of serofibrinous fluid. On changing the position of the patient from the upright to the horizontal, the dull triangle nearly or quite disappears unless the fluid is encapsulated. The respiratory murmur, the voice sounds, and fremitus are diminished over this area, but the changes are less marked than on the affected side. The character of the fluid appears not to influence the triangle.

FIG. 32




Aortic insufficiency; hydrothorax on the right side; paravertebral triangle of dulness on the left. (Thayer and Fabyan.)

The dull triangle is practically constant in the presence of free pleural

[1] The triangle was first noted by Korányi in 1897 (in the fourth volume, p. 717, of *Belgógyàszat Kezikönyze*, and again in Eulenberg's *Realenzyklopädie der gesamtem Heilkunde*, xiii). It was independently re-discovered and more fully described by Grocco (*Riv. crit. di clin. med.*, Firenze, 1902).

[2] *Riv. crit. di med.*, Firenze, 1904, v, 5, 21, 37.

[3] *American Journal of the Medical Sciences*, January, 1907.

fluid or of encapsulated fluid in contact with the spinal column. A small area of dulness on the side opposite a pneumonia has occasionally been observed. The writer has not observed it in pneumonia or in other conditions than pleural fluid.

In explanation of the phenomenon, Baduel and Siciliano suggest that fluid intervening between the spine and resonant lung inhibits the capacity of the former for sonorous vibrations, thus acting as a mute. The diminished resonance extends into the paravertebral region and increases in width from above downward, since the fluid at its base comes into wider contact with the spinal column and extends farther toward the opposite side. Displacement of the mediastinal contents and compression of the sound lung may play a part in its production.

**Blood.**—The number of red cells and the amount of hæmoglobin present no striking features beyond usually not more than slight grades of secondary anæmia.

*White Cells.*—In general, it may be said that the leukocytes in primary serofibrinous pleuritis are only rarely above normal in the absence of complications. Infectious pleuritis, on the other hand, is usually accompanied by leukocytosis. The white count, therefore, may be of value in distinguishing the two forms of the disease.

*Tuberculous Effusion.*—Of 33 cases of primary serofibrinous pleuritis in which tubercle bacilli were found in the fluid by inoscopy or animal inoculation the white count was above 12,000 in only 3 (9 per cent.), of whom 2 showed a leukocyte count of 14,000 to 15,000, and the remaining case 20,400. A complicating pulmonary tuberculosis may raise the white count, for of 32 cases in this group 7 (21.8 per cent.) were 12,000 or over. In 301 primary cases, of doubtful but probable tuberculous nature, the white count was 12,000 or over in 57 (18.9 per cent.). Of these 57 cases the leukocytes numbered 12,000 to 13,000 in 22; 13,000 to 14,000 in 9; 14,000 to 15,000 in 8; 15,000 to 16,000 in 3; 16,000 to 20,000 in 10, and 20,000 to 24,000 in 5. The leukocytosis was doubtless transient in many.

In 224 separate counts, in 20 cases of primary pleurisy, daily until discharge or disappearance of the fluid, Morse[1] found that only 13 counts went above 10,000. Of these, 9 were in 1 case showing pneumococcus infection at autopsy. The other 4 were in 2 cases, and the counts were but little above 10,000. He concludes from his study that there is no evident relation between the duration of the disease, the temperature, the presence of blood or few pus cells in the fluid, the amount of fluid or its variation and the leukocyte count.

*Infectious (non-tuberculous) Pleuritis.*—The *metapneumonic* effusions are, as might be expected, accompanied by an increase of the white cells. Of 28 cases in this class the leukocytes were above 12,000 in all but 6 (78.5 per cent.). They numbered 12,000 to 16,000 in 4; 16,000 to 20,000 in 6; 20,000 to 50,000 in 12. Pneumonia is not a necessary factor in raising the white count, however, and infection of the pleura alone in apparently uncomplicated cases with serofibrinous effusion may raise the white count, as in 2 streptococcus infections with 19,600 and 35,400 white cells.

Serofibrinous effusions complicating arthritis showed an increase of white cells in all of 3 cases, but it must be a question whether the leukocytosis can be ascribed to one or the other lesion.

[1] *American Journal of the Medical Sciences*, 1900, cxx, p. 658.

*Differential Count.*—Aside from the occasional presence of eosinophilia in hemorrhagic effusions, there appears to be nothing characteristic in the differential count in serofibrinous effusion. Of 17 cases, the relative proportion of white cells showed nothing remarkable with the exception of a relative increase in the polynuclear cells in cases with leukocytosis and an eosinophilia of 20 per cent. in 1 of 5 cases with bloody fluid.

**Spleen.**—This is rarely, if ever, enlarged unless some complication exists. It may be palpable from dislocation with left-sided accumulation.

**Axillary Glands.**—Due allowance must be made for the presence of small palpable glands in a large proportion of normal individuals. Rarely the axillary glands on the affected side may be enlarged by extension of the pleural disease, whether simple, tuberculous or malignant.

**Inequality of the Pupils.**—This may in rare instances occur from involvement of the sympathetic nerve. The difference in size is usually slight.

**Blood Pressure.**—This is usually normal with pleural effusions, compensation for intrathoracic pressure being maintained by increased respiration. When this compensation fails, however, there may be a fall of pressure. Capps[1] noted an increase of blood pressure during the excitement preceding thoracentesis. There was a constant fall during the withdrawal of the fluid, the average in 19 observations being 20 mm. Hg. Evacuation of large amounts of fluid, rapid withdrawal, long duration of the effusion, senile changes in the bloodvessels and heart, increased the fall of pressure.

**Radioscopy.**—This may confirm the results of physical examination, showing the limits of the effusion, the position of the displaced heart and the diaphragm. It may also show the presence of unsuspected pulmonary processes. It is especially valuable in locating an encapsulated effusion. The fluoroscope admits of examination from different points of view in rapid succession, but the radiograph is, in general, to be preferred. Permanent records, for study and comparison, are thus secured. The plates are more satisfactory if the patient can hold his breath during the exposure. Pleural adhesions may be suggested by a lack of diaphragmatic excursion. Thick pleura without fluid may be indicated by a lack of uniformity, by irregular limitation of the shadow and an absence of depression of the diaphragm and dislocation of the heart. The shadow is less dense than with fluid. In the presence of pleural fluid, the shadow is more uniform, more sharply outlined, and when the fluid is free occupies the lower part of the pleural space. Its upper border is curved, unless pneumothorax is present, when it assumes a hydrostatic level. A comparison of plates taken with the patient upright and lying down confirms the clinical observation of the mobility of fresh serofibrinous effusions. The shadow produced by serous is less dense than by purulent or hemorrhagic fluid.

**Complications.**—Lesions having an etiological relation with the disease have already been considered. It is difficult oftentimes during life or even at the postmortem table to separate them from conditions dependent on the pleuritis. These secondary processes only need be considered here. Tuberculosis may rarely extend from pleura to uninvaded lung. The progress is usually, however, from lung to pleura. Acute miliary tuberculosis may rarely complicate or follow serofibrinous effusion. Infection may extend to the opposite pleura, the pericardium, peritoneum, or other parts of the

[1] *Journal of the American Medical Association*, January 5, 1907.

body. Perihepatitis or perisplenitis may thus arise. Thrombosis of the pulmonary vessels, the venæ cavæ, heart, iliac, femoral, saphenous, or other veins may be associated with increased intrathoracic pressure and infection. Embolism may be rapidly fatal. Œdema of the lungs is a constant danger in large accumulations and with untapped effusions is probably due to cardiac insufficiency. Perforation of the lung or thoracic wall complicates purulent effusions with unfortunate frequency, but is rare with the serofibrinous form. It has been noted by Sahli[1] and Sokolowski. Nephritis probably bears only a chance relation to pleuritis. It arose under observation in only 1 of 500 cases in the writer's series.

**Causes of Sudden Death.**—Death may be due to associated and independent lesions to which the pleuritis is secondary. Such causes need not be considered here. Of causes dependent on the serofibrinous effusion, thrombosis and embolism are among the most frequent. The pulmonary vessels, the auricles, the venæ cavæ, iliac and femoral veins often contain thrombi, which may give rise to emboli, with rapidly fatal infarction of the lungs, as in 5 of 14 autopsies in the writer's series. Cerebral embolism is less common. Œdema of the lungs may be the only associated lesion found, as in one case with a double effusion. Postmortem examination does not always disclose the immediate cause of death, which has then been thought to be due to compression of the aorta (Trousseau), or to a kink or twist in the inferior vena cava (Bartels), but Osler in a number of observations was unable to substantiate the latter. Cerebral anæmia, from a mechanical hindrance to the circulation, is a possible cause. Pressure on the venæ cavæ, and the heart itself, especially the auricles, may embarrass the cardiac mechanism, resulting not only in cyanosis, rapid, feeble pulse, and dyspnœa, but even syncope and death. Various factors may operate in individual cases. Large double or left-sided effusions are more dangerous. Death may follow sudden change of position, an attack of pain, deep respiration, or a paroxysm of cough. Many more lives are sacrificed by hesitation and delay in thoracentesis than by the operation.

**Duration.**—In the writer's series of 369 cases of primary serofibrinous pleuritis, the time from the beginning of symptoms to discharge from the hospital was less than three weeks in 53, three to six weeks in 167, six to nine weeks in 60, nine to twelve weeks in 43, three to six months in 31, six months to one year in 12, two years or over in 3. Thus, about 60 per cent. ran their course within six weeks, about 87 per cent. within three months. The duration is longer with large effusions, in old and debilitated patients, in the presence of complications, in untapped cases or those in which evacuation is delayed. It is shortest in primary effusions, in young and otherwise apparently healthy individuals, treated by early tapping.

**Relapse.**—Although it is not uncommon after withdrawal of fluid for it to re-accumulate under observation and necessitate one or more tappings, it is rare for a serofibrinous effusion to re-appear on the same side after it has been fully absorbed or removed. In one of the writer's series, nine months elapsed between the removal of fluid and the appearance of the patent with an accumulation on the same side, but it is not certain that the fluid was fully removed at the first operation. The obliteration of the pleural sac following serofibrinous effusion is probably responsible for the rarity of true relapse.

[1] *Mitth. aus klin. und med. Inst. der Schweiz.*, 1894.

**Sequelæ.**—It is rare for serofibrinous effusions to change from serous to purulent fluid. Of 1185 cases in the writer's series, empyema developed in only 16 (1.3 per cent.). When empyema follows serofibrinous effusion, the fluid has usually been turbid, with an excess of polynuclear cells from the beginning. Spontaneous or artificial pneumothorax may occur, and, if the communication is through the lung, infection may follow. Imperfect technique in tapping may cause empyema. Slight dulness, diminished expansion, breathing, and fremitus last for a variable period after the disappearance of serofibrinous fluid. The intercostal spaces may be slightly narrowed and the affected side somewhat smaller. These changes may be permanent, but are less common and less marked than after empyema. The heart usually returns to its normal position. Rarely it may be fixed by adhesions in an abnormal position toward the sound side or slightly displaced toward the affected pleura. Slight lateral deviation of the spine may accompany these changes.

**Diagnosis.**—This is usually easily made from the onset with pain, the diminution or disappearance of which is accompanied by increasing dyspnœa, the diminished expansion of the affected side, initial narrowing, with later enlargement of the side and widened interspaces, the character and distribution of the dulness, diminished or absent breathing and fremitus, and the displacement of neighboring organs.

**Diseases with which an Effusion may be Confused.**—1. INTRATHORACIC. (*a*) *Thick Pleura.*—Following the partial or complete absorption or removal of pleural fluid, the thickened pleura may give rise to some confusion. There may be slight dulness, diminished breathing and fremitus. The side is not flat, however, the breathing only slightly altered, without bronchial character, and the fremitus, although it may be diminished, is not absent. The paravertebral triangle of dulness opposite the affected side is absent and the heart is not displaced.

(*b*) *Pneumonia.*—Typical lobar pneumonia is easily differentiated by its more severe onset, with chill and rapid rise of temperature, cough with rusty sputum, dulness (not flatness), bronchial breathing, increased voice, whisper and tactile fremitus, and consonating rales. The signs are often confined to parts or the whole of one or more lobes. Atypical pneumonia may closely simulate effusion. Cough and expectoration may be absent. Partial or complete involvement of the lower lobes with occlusion of the bronchi by secretion (massive pneumonia) may give rise to signs of effusion. If the bronchi can be emptied by cough, the signs may then become clear. The absence of cardiac displacement is important. Small amounts of pleural fluid often complicate pneumonia. Small effusions are more often serofibrinous, large amounts more commonly purulent. In doubtful cases exploratory puncture should not be delayed. Chronic suppurative changes in the lungs, with multiple bronchiectatic cavities, interstitial pneumonia and thick pleura, may closely resemble pleural effusion. The vocal fremitus may be diminished; in rare instances it may be absent, if the dilated bronchi are filled with secretion. Evacuation may be followed by a return of fremitus. The dulness is often greater in some places than in others, and is not as marked as with fluid. The side may be contracted, the interspaces somewhat narrowed, and the heart in normal position or slightly displaced toward the affected side. The diaphragm may be elevated, the diaphragm phenomenon diminished in amplitude or absent. Exploratory puncture is attended

with some danger of perforating the elevated diaphragm and infection of the peritoneum, of bleeding from injured bloodvessels or granulation tissue, or the infection of an intact pleura in the withdrawal of the trocar. If pus is found, it may come from pulmonary cavities.

(c) *Tumors of the Lung and Pleura.*—Tumors which reach the periphery of the lung may give rise to some confusion. There may be flatness, diminished or absent breathing, and fremitus. The site and contour of the process may differ from pleural fluid. Bloody sputum, dyspnœa, stridor, paralysis of the vocal cords, dysphagia, dilatation of the cervical or thoracic veins and superficial metastases may be suggestive. If the pleura is invaded by the new growth, an effusion is common and this may mask the pulmonary process. Exploratory puncture may evacuate bloody fluid. Echinococcus of the lung or pleura may simulate serofibrinous pleuritis.

2. Abdominal Affections.—Subdiaphragmatic abscesses and tumors, especially echinococcus cysts, may simulate an accumulation of pleural fluid. Abdominal pain, tenderness, and muscular spasm may be due to diaphragmatic pleurisy.

**Determination of the Character of Pleural Fluid.**—This is impossible in most instances without exploratory puncture, but certain suggestive features may be mentioned. Hydrothorax is most easily distinguished from the presence of cardiac or renal disease or both, bilateral fluid, which shifts more readily on changing the position of the patient, and œdema elsewhere, as well as absence of pain, fever, leukocytosis, and friction rub. In unilateral hydrothorax without general dropsy the distinction may be impossible. Hemorrhagic fluid may be suspected following trauma, when the effusion is secondary to malignant disease, or with an eosinophilia in the circulating blood. Chylothorax can hardly be distinguished, but may be suspected with the known presence of chylous ascites. Empyema, in typical cases, may be differentiated. It is more likely to be secondary and metapneumonic, while serofibrinous effusion is much more likely to be primary. If the patient is a child and under five years, the chances are much in favor of pus. The symptoms are of little assistance in individual cases, but in general are more severe in empyema, with higher and more irregular fever, chills, sweats, and more rapid loss of flesh, strength and color. Œdema of the skin, dilatation of the superficial veins, thoracic pulsation, perforation of the lung or other organs may suggest empyema. A leukocytosis above 12,000, unexplained by other features, suggests an infectious process and usually means pus.

Exploratory Puncture.—A needle and syringe are commonly used. The needle should be 6 cm. long, with an internal diameter of at least 0.5 mm. The syringe should be capable of holding from 5 to 10 cc., and is preferably of glass, with all glass or glass and asbestos piston, thus permitting satisfactory sterilization without damage. It is well to connect needle and syringe with rubber tubing to avoid breakage of the latter and pain at the site of puncture. The rubber tubing should be thick enough to stand negative pressure without collapse. Because of the smallness of the needle compared with the trocar, it causes less pain. There is said, also, to be no danger in the puncture of the lung or diaphragm with a small needle.

The apparatus recommended for aspiration, the writer believes, is to be preferred. A small trocar is hardly more painful than the needle. If pneumothorax and possible infection of the pleura are to be avoided, a

plugged needle must be withdrawn for the removal of the obstruction, while with the air-tight trocar fibrin or other material may be readily dislodged by the stylet without the withdrawal of the instrument. If the lateral outlet of the trocar is guarded with a stop-cock, the syringe may be filled, then removed after the lateral outlet is closed by the stop-cock and replaced for the evacuation of more fluid.

If aspiration is decided on, Potain's apparatus can be attached to the lateral outlet and the discomfort of another puncture is avoided. Thick pus may fail to flow through a small needle.

The method of performing exploratory puncture does not differ from that for thoracentesis. In addition to the determination of fluid, the operator may appreciate any unusual thickness or density of the pleural or pulmonary tissue by the amount of resistance encountered by the instrument (palpatory puncture). In rare instances a diagnosis between pleural and subdiaphragmatic fluid may be made. By the removal of the syringe from the rubber tube attached to the trocar, the apparatus is converted into a siphon and the amount of pleural pressure may be determined, as suggested by Krönig. The normal depression during inspiration and elevation during expiration of the column of fluid may be reversed in subdiaphragmatic collections. The withdrawal of small amounts of fluid by exploratory puncture is occasionally followed by rapid spontaneous absorption of what remains.

In rare instances, if the needle is used for exploratory puncture, the microscopic examination of a piece of tissue caught in the lumen may furnish the diagnosis. In one of the writer's series a tubercle was thus demonstrated. Prentiss[1] made the diagnosis of sarcoma and Steele and Girvin[2] of carcinoma of the pleura by this means.

**Examination of Pleural Fluids.**—Under normal conditions there is merely enough fluid within the pleural sac to lubricate the apposing surfaces of the pleuræ, and as yet no chemical analysis of this has been made.

1. CHEMISTRY.—Pleural fluid may be *serous;* it may contain varying amounts of fibrin, when it is known as *serofibrinous;* it may also vary in its content of blood and pus and may then be termed *hemorrhagic, fibrinopurulent,* or *purulent.* The presence of chyle justifies the term *chylous;* of fat not due to chyle, *chyliform.* Clear serous fluids are usually yellowish, often reddish from the admixture of blood, and at times somewhat greenish in color. In the presence of jaundice the fluid is more deeply colored and responds to the tests for biliary substances. Pleural fluids may be turbid from albumin in fine subdivision, fat or fibrin, in the form of flocculi or pus. Such fluids vary in color from white through shades of yellow and reddish to green. Large quantities of blood or pus are usually sufficiently obvious from the gross appearance.

*Transudates and Exudates.*—It is customary to make a clinical distinction between fluids resulting from hydræmia and stasis or transudates and those arising in the course of inflammatory processes or exudates. Such fluids may be due to one or more different factors, as in similar accumulations elsewhere. It will suffice here merely to refer to the probable influence of filtration and osmosis and an increased permeability or possible

[1] *Transactions of the Association of American Physicians,* 1893.
[2] *Proceedings of the Pathological Society of Philadelphia,* 1901.

secretory power of diseased capillary walls, concerning the ultimate bearing of which, however, little is definitely known. The chemistry is of principal interest in furnishing data which may confirm a clinical diagnosis of hydræmia, stasis, or inflammation as a cause.

In general, transudates are of relatively low specific gravity and contain a small amount of albumin, *i. e.*, a specific gravity of 1010 or under for hydræmic fluids, with traces to 1 per cent. of albumin; and 1010 to 1015 in venous transudates, with 1 to 3 per cent. of albumin. The albumin is principally serum albumin, serum globulin, and a trace of fibrinogen. Only a very slight precipitate follows the addition of a few drops of acetic acid to the fluid. It coagulates slowly or not at all, unless mixed with blood. The specific gravity of exudates, on the other hand, is usually 1018 or higher, with 4 per cent. or more of albumin. They show a more abundant precipitate on the addition of acetic acid, contain a larger amount of fibrinogen, and usually coagulate rapidly with or without the presence of blood. For the estimation of albumin Esbach's test may be used, but is only approximately accurate, and for more exact determination more complicated methods must be employed, such as the weight of the precipitated proteid or the total nitrogen (Kjeldahl).

2. Cytology.—*Cytodiagnosis.*—By this is understood the determination of the cause of the effusion from the character and numerical relation of its cellular elements.

*Technique.*—The fluid should be examined as soon as possible after withdrawal. To prevent spontaneous coagulation and the entanglement of cells in the meshes of fibrin, it may be placed at once in a sterile flask containing about one-third to one-half its volume of 1 per cent. sodium citrate in 0.85 per cent. salt solution. If coagulation has already occurred, Widal recommends agitation with glass beads to dislodge entangled cells, but such a procedure may give less accurate results than the examination of fluid in which clotting has not taken place. The sediment is obtained by centrifugalization, the supernatant fluid carefully decanted, and thin smears made with the platinum loop. These are allowed to dry in the air or over the Bunsen flame. Care must be taken not to burn the preparation.

Fixation and staining may be done in various ways. The writer has found the following method satisfactory: Wright's[1] blood stain is allowed to remain on the cover-glass from one-half to one minute, then diluted with 8 to 10 drops of water, and allowed to stand one to two minutes. The preparation is washed in a gentle stream of tap water, dried over the Bunsen flame, and mounted in balsam.

Red cells are of relatively little importance in the microscopic examination. A differential count should be made of the white cells, which may be classed as follows:

*A.* Polynuclear: (*a*) Neutrophiles; (*b*) Eosinophiles; (*c*) Mast-cells.

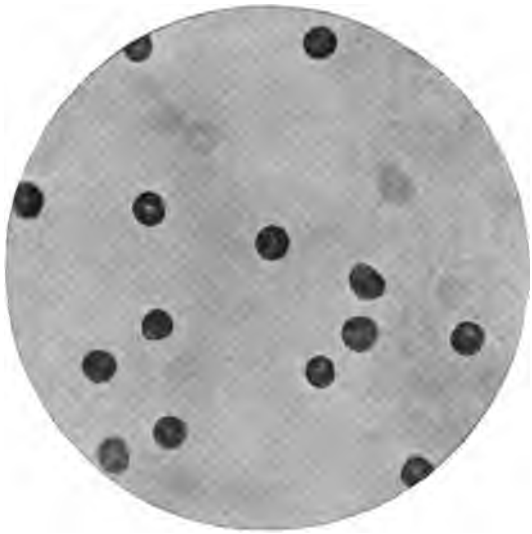
*B.* Mononuclear: (*a*) Lymphocytes; (*b*) Endothelial cells; (*c*) Cells intermediate and indistinguishable from (*a*) and (*b*).

Polynuclear neutrophiles correspond to similar cells found in the circulating blood. Degenerative processes may lead to the formation of isolated nuclear fragments, with or without a granular protoplasm, contraction of the nucleus alone or both nucleus and protoplasm, and vacuolization. Such

[1] *Journal of Medical Research*, January, 1902.

changes, however, seldom modify the character of the cells to such an extent as to prevent their recognition. Eosinophiles are often found in

FIG. 33



**Lymphocytosis** Case of primary tuberculous pleurisy. x 750 (Musgrave.)

FIG. 34

**Large phagocytic endothelial cells and polynuclear leukocytes.** Case of acute infectious pleurisy. x 750. (Musgrave.)

small numbers, mast-cells less often. Both are in most instances readily classified. Of the mononuclear cells, typical examples of lymphocytes and endothelial cells are easily differentiated. The lymphocytes correspond to similar cells in the blood. At times, no rim of protoplasm can be detected about them. Endothelial cells are large, flat, irregular, round, or oval in contour, with a round or oval blue nucleus, which is poor in chromatin and often vacuolated. They may be isolated or in plaques, the so-called "Placards endothéliaux." Such an arrangement as the latter plainly indicates their origin from the pleural wall. They are phagocytic, and have in consequence been called macrophages. Considerable variation is common in nucleus and protoplasm. Either or both may be markedly vacuolated and one or the other may be absent.

FIG. 35

Endothelial plaques and cells. Case of hydrothorax due to cardiac disease. × 750. (Musgrave.)

Unfortunately, between typical examples of lymphocytes and endothelial cells there are atypical forms of mononuclear leukocytes which cannot be fairly classed with either of the two groups. Widal believes that in the absence of degenerative changes, endothelial cells can be differentiated from lymphocytes by the character of the nucleus—a distinction which is not believed to be possible by the writer in common with many other observers. Such atypical cells, however, usually comprise but a small proportion of the white cells, and may thus introduce a negligible error in the differential counts. In some cases, the classification of the cellular elements is impossible because of degenerative changes.

*Cytological Formulæ.*—The varying character of cells in pleural fluids was first noted by Ehrlich. Further observations were made, among

others, by Quincke and Wolff. In 1900, Widal[1] elaborated the method, formulated a classification of pleural diseases, based on the varying proportion of different cells in pleural fluids, and suggested the term "cytodiagnosis." Widal stated that (1) a predominance of polynuclear leukocytes means an effusion of infectious origin (pneumococcus, streptococcus, staphylococcus); (2) of lymphocytes, a tuberculous effusion; and (3) of endothelial cells, especially if in plaques or sheets, an effusion of mechanical origin.

More recent observations make it probable that the character of the cells in pleural fluids depends not only on the cause of the process, but also on the intensity of the pleural reaction. The predominance of one type of cell, therefore, cannot be regarded as a specific indication of an infectious, tuberculous, or mechanical origin, although Widal's formulæ have been sufficiently verified to warrant a probable diagnosis, provided the clinical character of the case accords with the microscopic findings. The method is thus a valuable accessory in diagnosis, but must not be expected to establish the diagnosis of itself alone.

Various exceptions to the above formulæ must be noted. They limit the diagnostic value of the procedure. An excess of polynuclear leukocytes in infectious pleuritis is subject to least variation. Concerning the lymphocytosis of pleural tuberculosis, it should be noted that a transient excess of polynuclear neutrophiles has been found by Widal and others in its early stages. The secondary infection of a pleura already the site of tuberculosis may likewise modify the character of the cellular elements, with an increase in the relative proportion of polynuclear cells. In regard to the predominance of endothelial cells in mechanical effusions, it has been noted that they are relatively most numerous in the early stages of the disease. In long-standing transudates, Naunyn[2] has shown that the proportion of endothelial cells may diminish and lymphocytes may be in excess. Lymphocytosis has been present without a reaction to tuberculin and in transudates shown by autopsy not to be tuberculous. As in fluids with lymphocytosis, so, also, in those with an excess of endothelial cells, an infection may raise the number of polynuclear cells.

In malignant disease of the pleura, the cellular elements conform more nearly to those found in mechanical effusions, with an excess of endothelial cells, but large numbers of spindle cells may suggest sarcoma, as in Warthin's case. Examination of the fluid in conjunction with the history and physical examination may confirm an otherwise doubtful diagnosis.

In experiments on animals, a lymphocytic pleuritis has been produced by the injection of diphtheria bacilli and diphtheria toxin. The bearing of such experiments on cytodiagnosis is still an open question.

3. Bacteriology.—For the demonstration of the pneumococcus, the pyogenic cocci, and other organisms capable of cultivation, smear preparations should be made and suitable media inoculated.

*Tubercle Bacillus.*—Special methods, the results of which have already been mentioned under Etiology, have been devised for its demonstration.

*Inoscopy.*—Jousset,[3] in 1903, proposed a simple method for the demonstration of tubercle bacilli in coagulable fluids. After withdrawal, the fluid, at least 100 cc. in amount, is allowed to clot. The clot is removed and

[1] Widal and Ravaut, *Compt.-rend. de la Soc. de biol.*, 1900, p. 648.
[2] *Deut. med. Woch.*, 1903, 18 V. B., p. 140.
[3] *La semaine méd.*, 1903, p. 22.

washed free of serum on sterile gauze, with sterile water, then placed in a flask containing 10 to 30 cc. of the following digesting fluid: Pepsin, 1 to 2 grams, pure glycerin and strong hydrochloric acid of each 10 cc., sodium fluoride 3 grams, and distilled water to 1000 cc. The flask is placed in the incubator at 38° C. until the clot is digested. Two to three hours are usually needed. Frequent agitation of the fluid hastens the process. The digested fluid is sedimented, the supernatant fluid decanted, and from the precipitated material smears are made with the platinum loop. These are dried and stained for tubercle bacilli.

*Sedimentation.*—Zebrowski[1] takes at least 100 cc. of fluid, adds an equal volume of 1 per cent. sodium fluoride to prevent coagulation, and allows the solution to stand in a cool place for twenty-four hours. The supernatant fluid is decanted and the precipitate centrifugalized. Smears made from the material thus obtained are investigated for tubercle bacilli, as already described. The greatest care should be taken that bacilli in fluids previously examined are not left clinging to the apparatus.

*Animal Inoculation.*—All instruments must be sterilized. Intraperitoneal inoculation of guinea-pigs is most successful. For the demonstration of tubercle bacilli, large amounts of fluid must be injected, but in divided doses. If the animal lives, three months should be allowed to elapse before the examination is made. Le Damany[2] made injections each week of 10 to 50 cc. of fluid, varying the amount according to the toxicity of the fluid, and was thus able to inoculate as much as 300 cc. The fluid was preserved in test tubes of small calibre, then transferred to a medium-sized tube, open at both ends, one of which was drawn to a blunt extremity and inserted through a small abdominal incision. Escape of fluid about the incision was prevented by a U-shaped suture. If the fluid failed to flow, the free end of the tube was plugged with cotton and carefully heated, thus insufflating the contents. In this way both clot and sediment were inoculated.

**Prognosis.**—In general, the immediate prospect in serofibrinous pleuritis is good. Large or double effusions may, however, be suddenly fatal. Of 500 cases in the writer's series, 4 (0.8 per cent.) died without other obvious cause than the effusion. In one, large amounts of fluid rapidly re-accumulated, conforming to the uncommon variety known as pleuritis acutissima. No autopsy was obtained. The three remaining patients were not tapped. Two had double effusions, in one of whom autopsy showed that death was due to pulmonary embolism; in the second no other cause of death was found postmortem than œdema of the lungs. In the last patient there was a large unilateral accumulation, and examination after death showed pulmonary embolism. Thoracentesis might have been life saving in these cases. If an infectious and non-tuberculous cause can be established, the prognosis is favorable.

**Prophylaxis.**—In a large majority of the cases this embraces measures for the prevention of infection with the tubercle bacillus and other organisms. Pleural fluids should be carefully handled by the physician to avoid contagion.

**Treatment.**—1. **The Natural or Spontaneous Cure.**—The large proportion of cases coming to autopsy with pleural adhesions, associated with fibro-

[1] *Deut. med. Woch.*, 1905, Nr. 36.
[2] *La presse médicale*, November 24, 1897, p. 329.

caseous or calcified pulmonary lesions, shows that pleural disease, directly or indirectly dependent on the tubercle bacillus, is frequently arrested or healed. Tuberculous nodules in the pleura, as elsewhere, may be walled off by a dense envelope of fibrous tissue, and thus prove of little danger to the individual, forming latent foci. Calcification may take place, as in 5 of 27 cases (M. G. H.), with obsolete tuberculosis as a result. Tuberculous granulations in a part or the whole of the pleura may finally be converted into firm, fibrous tissue, ending in obliteration of the pleural sac and no further trouble from the process. The clinical history of cases of certain or probable pleural tuberculosis shows that recovery is not infrequent.

2. **General Measures.**—For purposes of treatment, as Osler has said, it is best to assume every case to be tuberculous, unless there is good reason to believe otherwise. Fortunately, many patients are still in fair health when they first come under observation. The course of the disease is often slow and spontaneous recovery frequent, which, indeed, too often fosters half-way measures in its care. As in tuberculosis elsewhere, we must rely chiefly on rest, fresh air, and the improvement of nutrition. It must be constantly borne in mind that the pleural disease is usually secondary to tuberculosis of the lung or thoracic glands, as is shown by autopsy, although the primary focus often escapes detection during life.

If we are to secure the hearty coöperation of the patient, he should be frankly told the seriousness of his condition. We can otherwise hardly secure his acceptance of the necessary restrictions on his mode of life. According to our present knowledge his chances with primary serofibrinous effusion are about 3 or 4 in 10 that he will develop pulmonary or other tuberculosis within a period of six or seven years. These figures have this hopeful aspect, however, that they are for the most part gathered from cases in which treatment terminated with the disappearance of the effusion. They probably, therefore, represent the natural evolution of the disease, and a longer or even a permanent arrest may be expected in patients who can and will consent to more careful supervision and regulation of the daily life.

During the acute stage, while there is fever, rest in bed should be enforced and maintained until the temperature is normal. After the acute symptoms have subsided, the patient may cautiously be given greater liberty, careful watch being kept meanwhile on the temperature. The supply of fresh air should be continuous and abundant, by night as well as by day. Means similar to those in pulmonary tuberculosis may be taken to secure this. In undernourished individuals an increase in weight should be sought from the beginning of treatment, and for such patients extra feeding must be employed. The food should be simple and nutritious and extra feedings of milk or eggs may be given between the regular meals. Fat is important and is best given in the form of cream or fresh butter.

The treatment should not end with the subsidence of fever and the disappearance of fluid. Patients who have apparently recovered should be kept under observation, and every effort made to maintain the general condition at a high level. Country is better than city life. The occupation should be carefully chosen. Overcrowded, dusty, or badly ventilated places should be avoided. Indiscretion and neglect may bring the patient under observation a second time with pulmonary or other tuberculosis too late for successful treatment. Loss of weight, fever, cough, or other sus-

picious symptoms should receive immediate attention, and, if necessary, a further course of rest, outdoor life, and extra feeding.

3. **Local Applications.**—These are for the alleviation of symptoms. The ice-bag, hot-water bottle, and hot applications repeated every two hours may efficiently relieve pain, for which, however, morphine may be necessary. Counterirritation has frequently been used. It is doubtful if blisters have other than a harmful effect, making the patient uncomfortable and adding to the danger of thoracentesis, if the skin becomes infected. Strapping the affected side has been suggested, but only further displaces the lung and other organs. It may actually hinder absorption by compressing the lymph channels.

4. **Special Measures.**—THORACENTESIS.—*Indications.*—In general, the opinion of the present time is in favor of tapping serofibrinous effusions (1) with pressure symptoms, such as severe dyspnœa, cyanosis, or rapidly developing cardiac weakness; (2) of large amount, with dislocation of heart and mediastinum, even without pressure symptoms, and (3) of medium amount when other means have failed to bring about absorption and two or three weeks have elapsed.

With (1) *pressure symptoms and* (2) *large effusions, thoracentesis is imperative* and should be done without delay. It has been the unfortunate experience of many physicians to decide on evacuation of such cases within a given time before the expiration of which the patient has suddenly died. The presence of fever is not a contra-indication. Left-sided effusions are somewhat more dangerous. Bilateral fluid, of only medium amount, should likewise be immediately evacuated. Concerning the indications for the removal of effusions of (3) medium amounts, there is a division of opinion. Delay and trial of other means for two to three weeks is the customary procedure, but there has been a tendency lately to resort in these cases to early tapping.

*Should Medium and Small Effusions be Tapped?*—In favor of the customary delay before resort to tapping, it may be said that medium and small effusions are often spontaneously absorbed. The operation causes apprehension and pain, and is dangerous in a small proportion of cases. On the other hand, early tapping allows the lung to return to its normal position and removes fibrinous material which may hinder absorption. Retraction or compression from fluid and the formation of fibrous tissue in and about the lung may prevent full re-expansion and favor thoracic contraction and restriction of the breathing capacity. It may also favor the extension of tuberculous or other lesions within the lung or the pleura. Return of displaced organs to their normal positions relieves an embarrassed circulation, promoting absorption and repair. That tapping actually shortens the duration of the disease is suggested by a comparison of the stay in hospital of tapped and untapped cases. Of 15 uncomplicated cases in the Pennsylvania Hospital,[1] in which the effusion was removed by tapping, the average duration with effusions occupying one-third of the cavity was 15.4 days; for 39 cases, with effusions occupying two-thirds, 20.1 days; while in 17 cases in which the chest was one-third full and not tapped, the duration was 21.8 days; in 15 with two-thirds, 24.3 days. Delafield, in 1902, strongly favored thoracentesis not only for the removal of

[1] Fraley, *American Journal of the Medical Sciences*, May, 1907.

fluid, but to cure pleurisy as a morbid process. He reported 200 cases. Referring only to the immediate results, 182 left the hospital "entirely cured," 6 left within ten days after aspiration and probably recovered; 6 left at periods of from seventeen to thirty-six days with the pleurisy better, but the results were uncertain and 6 were not improved. In 64 cases the patient left the hospital well within a week of the aspiration, 138 within two weeks. There were no deaths.

*Selection of Cases for Tapping.*—The character of the fluid is important in the decision between thoracentesis and thoracotomy. With clear fluid, thoracentesis is the operation of choice. Open incision is followed by suppuration, which is to be avoided. With turbid fluids the decision is more difficult. They are on the border line between serofibrinous and purulent effusions. Of 27 cases in the writer's series with turbid fluid containing an excess of polynuclear cells, 15 were cured by thoracentesis alone. In 12, pus was found at later tapping and thoracotomy was performed. The tendency of pleural fluid to sediment within the chest must be remembered. A sample from the upper layer may be turbid, while pus may exist below. Turbid fluids secondary to lobar pneumonia or due to the pneumococcus are relatively favorable for thoracentesis. With merely an excess of polynuclear cells in the differential count, tapping alone may be considered. Pneumococci may be found in such exudates, but are often incapable of cultivation. With abundant or necrotic leukocytes and pneumococci on cultivation, operation is usually necessary. Streptococcus infections are usually purulent, or rapidly become so, and generally demand open incision. The general symptoms, the amount of fluid and rapidity of re-accumulation must also be considered.

*Apparatus.—Needle or Trocar?*—The needle is simple and less expensive, but has two drawbacks. Its unprotected point may wound the expanding lung or the diaphragm. More important than this, however, a bit of tissue punched out during insertion or a small mass of fibrin may effectually occlude its lumen. To dislodge such particles, the needle must be withdrawn, if the danger of pneumothorax and possible infection of the pleura are to be avoided. Krönig[1] has devised a satisfactory needle, the point of which is rendered harmless by thrusting forward an enclosed and blunt-pointed cannula. The trocar with lateral outlet presents a harmless, blunt end after the removal of the stylet and can be thrust farther in, elevated or depressed without danger to neighboring structures. If plugged, the obstruction is readily removed by the insertion of the stylet and without danger of pneumothorax, if the packing is tight, as it should be, about the stylet. A negative puncture with an ordinary needle is less reliable than with the trocar.

Various trocars have been devised. The cannula of silver to avoid rust should be at least 7 cm. long. In general, the internal diameter should not exceed 1.5 to 2 mm. It is advantageous to have several sizes at hand. The stylet should fit tightly at the extremity of the cannula, which should taper gradually to a thin edge to avoid difficulty and pain in its introduction. A lateral outlet is needed for thoracic puncture, in order that the stylet may be moved in and out without disturbing the connections. A stop-cock on the lateral outlet is useful. Toward the proximal end of the instrument and this side of the lateral outlet there should be a stop-cock, to guard against leakage of air about

[1] *Berl. klin. Med.*, 1906, ii, pp. 131–5.

the entrance of the stylet and to maintain the instrument air-tight if the latter is removed. The stylet should run through a compartment capable of air-tight connection with the instrument and the play of the stylet through this compartment should also be air-tight in order that it may be moved in and out without danger of producing pneumothorax. The proximal end carrying the stylet is the weak part of the apparatus, since it is difficult to secure an air-tight all-metal connection without making the instrument too cumbersome and without the use of oil. The introduction of rubber washers, although they need to be frequently changed, is the most satis-

FIG. 36

Siphonage. (After Hoppe-Seyler.)

factory solution. The writer uses an air-tight trocar, constructed on the principles mentioned, with stop-cock on lateral outlet and cannula.

*Methods.*—In general, there are only two safe and reliable methods, *i. e.*, siphonage and aspiration.

1. *Siphonage.*—This is readily carried out. A trocar such as that described above or Krönig's needle may be used. A rubber tube about 75 cm. long, a clamp for the latter, a glass funnel, sterile water or salt solution are also needed. If the trocar is used, one end of the tube is fastened to its lateral outlet, the other to the glass funnel, by means of which the apparatus

is filled with the sterile solution. When the instrument is full, escape of the solution is prevented by fastening the clamp on the rubber tube or closing the stop-cock on the lateral outlet. The tube now contains a column of water, which, on the release of the clamp or stop-cock, is capable of exerting sufficient aspiratory force to overcome a negative pressure in the thorax under any ordinary conditions. The trocar is inserted into the chest while the free end of the rubber tube is held beneath the surface of the sterile solution, thus preventing aspiration of air, provided the negative pressure within the chest should be greater than the weight of the column of water in the rubber tube. By this method there is no danger of an excess of negative pressure, which may be varied at will by simple elevation and depression of the free end of the tube. Krönig attaches the free end of the rubber

FIG. 37

Krönig's method.

tube to a glass tube passing nearly to the bottom of a flask partly filled with sterile solution, and with a curved outlet at the top (Fig. 37). There is no danger of the entrance of air or of reflux of contaminated fluid. The pressure of the pleural fluid may be measured by elevation and depression of the flask, noting the difference between its upper level in the flask and the chest, when equilibrium is established.

2. *Aspiration.*—The most satisfactory method is by means of a bottle, connected on the one hand with the chest and on the other with an aspirator by means of rubber tubing. Aspiration may be effected by means of a pump, as in Potain's method. A rubber bulb may be used, as in Alexander's[1] modification of Unverricht's method. Fürbringer[2] secures negative

[1] *Deut. med. Woch.*, 1893, Nr. 10, S. 241.
[2] *Berl. klin. Woch.*, 1888, Nr. 13. S 254.

pressure in the bottle by aspiration with the mouth, which can hardly be recommended. In Dieulafoy's rack aspirator[1] the evacuated fluid flows directly into the vacuum apparatus. Stinzing[2] recommends a tall, graduated flask for the reception of the fluid. In both Stinzing's and Fränkel's[3] articles a full description and discussion of various instruments will be found.

Potain's apparatus is in most general use. The pump is capable of a dangerous degree of aspiratory force. Only sufficient aspiration should be used to just maintain the flow. The rubber tubing should be thick and all connections must be air-tight. A piece of glass tubing inserted between the trocar and bottle will be of assistance in noting the result of aspiration. If desired, a mercury manometer may readily be connected with the bottle, thus

FIG. 38

Aspiration with Potain's apparatus. (After Hoppe-Seyler.)

measuring the negative force. An extension of the inlet to the bottom of the bottle will prevent any back flow of air, provided the negative pressure within the thorax becomes greater than within the bottle. As a receptacle for the fluid a bottle of the proper size to fit the rubber stopper, graduated at different levels by marks of a file and capable of holding from 1500 to 2000 cc., should be chosen. The glass should be of such a quality as to stand sterilization without breaking.

*Technique.*—The instruments should be sterilized just before use. The trocars, all rubber tubing, rubber stopper to the bottle, scissors, and hypo-

[1] *A Treatise on Pneumatic Aspiration*, London, 1873.
[2] *Handbuch der Therapie innerer Krankheiten*, 1902, Band iii.
[3] *Handbuch der physikalischen Therapie*, Theil ii, Band i, Goldscheider und Jacob, 1902.

dermic syringe, if this is used, should be boiled. Disinfection with antiseptics is uncertain, and may interfere with subsequent bacteriological tests of the fluid. The operator's hands should be scrubbed clean and disinfected with alcohol. The patient's side should be prepared over a wide area with soap and water, using a piece of sterile gauze in place of a brush. It is then dried with sterile gauze and disinfected with alcohol. If operation is not at once undertaken, a pad of sterile gauze should be applied. The apparatus should be set up, tested by the aspiration of sterile water, and the air in the bottle should be under negative pressure before the puncture is made. The site chosen for puncture will vary with the amount and position of the effusion, and the pathological conditions. The position of the heart must be known. An encapsulated exudate must be sought with due regard to anatomical landmarks. With large or medium and free effusions, the puncture may be made in the fifth or sixth intercostal space in the midaxilla, with small effusions in the seventh space between scapular and posterior axillary lines. The choice of the latter situation has certain advantages, in that the patient is not disturbed by seeing the procedure and the trocar will be nearer the lower level of the fluid. The diminishing width of the intercostal spaces as the spine is approached may prevent the selection of a more posterior site. As the dome of the diaphragm rises normally as high as the fourth interspace in the nipple line, the sixth rib in the midaxilla and the eighth rib in the scapular line, a lower level cannot safely be chosen. In fresh effusions, the lung, the heart, and the diaphragm are displaced away from the selected site, and there is little danger of their injury, but with chronic cases, with narrowing of the interspaces, contraction of the side and elevation of the diaphragm, a higher level should be selected. The interspaces should be carefully counted before the operation is undertaken. A thickness of 2 to 4 cm. or more under ordinary conditions must be allowed for the thoracic wall. In fat subjects, or in the presence of a thick layer of fibrin, the trocar may fail to find fluid even at this distance. The patient is best placed on the bed to avoid unnecessary exertion after the operation. There is some advantage in performing the puncture with the patient in the sitting position, in which with small and free effusions the fluid may reach farther toward the front. The intercostal spaces may be widened by placing the hand of the affected side on the opposite shoulder. *Local anesthesia* may precede the operation and the subcutaneous injection of morphine has been advised, but may inhibit symptoms which would otherwise warn the operator of approaching danger.

As a guide for the *introduction of the trocar*. the selected interspace is palpated by the fingers of one hand, while in the other the trocar is held with the blunt end of the stylet firmly against the palm and the end of the index finger about 4 cm. from the point, thus guarding against too deep an initial puncture. The instrument is introduced by a quick thrust, perpendicular to the surface, just above the rib, to avoid the intercostal artery. It is pushed in until from the lack of further resistance the operator may judge that the point has reached fluid.[1] Insertion during forced inspiration may

[1] It is convenient to know that at the level of junction of the third costal cartilage with the sternum (sixth dorsal vertebra), the distance from the skin to the bloodvessels at the root of the lung in an average adult male was found by Piersol (Musser, *Journal of the American Medical Association*, January 5, 1907) to be 7 cm. in the midaxillary line on the left side and at a greater depth in other regions of the same transverse section.

depress the diaphragm out of danger when a low site is chosen. Preceding *withdrawal*, the operator may conveniently appose a piece of sterile gauze, enclosing the trocar, firmly against the region of puncture. The cannula should be quickly withdrawn. Rarely pleural fluid may continue to flow from the wound. Slight bleeding from the injury of small bloodvessels may occur. Pressure usually suffices to stop this, but if necessary, a stitch may be taken through the wound. A *dressing* may be made from a small pad of sterile gauze cut to an appropriate size and held in place by a single and larger layer fixed to the chest with collodion. This is better than adhesive plaster, the cleanliness of which is difficult to secure.

The trocar and rubber tubing should be cleaned at once after the operation. This is conveniently done by running first cold water, then alcohol, and finally ether through the apparatus, which should be dry when put away.

*Symptoms and Difficulties during Evacuation.*—Faintness and vertigo are not uncommon, and are usually due to psychic disturbance. They may be relieved by placing the patient in the reclining position and giving an alcoholic drink. An occasional slight cough is frequent toward the end of the evacuation. If severe, the operation should be stopped. Cough may be due to pleural irritation, to hyperæmia, or œdema of the expanding lung. If it persists, morphine may be given. Blood may rarely be expectorated during evacuation. It may arise from the rupture of small bloodvessels in the lung, from congestion, or from puncture of the lung with the trocar, and when it occurs it is best to discontinue the operation. Pain is not common, but if severe, is a contra-indication to continuance, as it may indicate undue tension on pleural adhesions. There may be a feeling of dyspnœa and general discomfort, perhaps cardiac in origin, and severe enough to warrant a halt in the operation.

The operator may have difficulty in inserting the trocar between narrow interspaces and a smaller instrument may be necessary. Unexpected movement on the part of the patient may direct the point of the trocar against a rib. After introduction and the withdrawal of the stylet, no fluid may follow. A bit of fibrin may have closed the opening, or if, after re-introduction of the stylet, the puncture is still negative, the trocar may need to be inserted farther, in a different direction, or partially withdrawn. The presence of firm tissue in the track of the instrument can usually be appreciated as a resistance against forward or lateral motion. Introduction elsewhere may be more successful. Finally, there may be no fluid, but negative punctures never positively exclude it. Interruption of the flow during evacuation may be due to fibrin, apposition of lung or diaphragm against the end of the cannula, or equalization of pressure within and outside the chest. The last may happen even with considerable fluid remaining, provided the lung is firmly bound down in a retracted position.

*Amount of Fluid to be Withdrawn.*—This depends on the size of the effusion. It has not infrequently been noticed that absorption followed removal of very small quantities. The rare occurrence of serious symptoms, and even of death, following the evacuation of large amounts of fluid is a warning not to be safely disregarded. With large effusions, as much as 1500 cc. may be withdrawn, provided no unfavorable symptoms arise during the process. Much larger quantities are often removed without an unfavorable result, and with very large effusions, in which the fluid runs without aspiration or symptoms, as much as 2000 cc. may be evacuated. If danger is

to be avoided, however, this amount should only rarely be reached and never exceeded. The remaining fluid will probably be absorbed; if not, the procedure can be repeated. With small effusions it is unnecessary to evacuate the last drop. Small amounts of fluid remaining are usually readily absorbed. The longer the effusion has lasted and the older the patient, the smaller the amount of fluid which can be safely withdrawn. More abundant adhesions and less elastic lung then increase the danger. In the presence of pulmonary tuberculosis, especial care should be exercised in the removal of fluid to avoid rupture of adhesions and artificial pneumothorax.

*Duration of the Operation.*—It is safer to evacuate fluid slowly. A half hour may be consumed in the removal of 1500 cc. in order that neighboring structures may gradually readjust themselves.

*Injections.*—The replacement of the evacuated fluid by air has been recommended. Filtered air, oxygen, and sterile salt solution have more recently been used. Air is said to be of advantage in the rare chronic cases in which adhesions prevent re-expansion of the lung following evacuation, or with bloody fluids in which negative pleural pressure only leads to renewed hemorrhage. Absorption of the air takes place slowly. Barr[1] replaces the evacuated fluid by about two-thirds to three-fourths of the original volume with filtered air, and finally injects 4 to 8 cc. of a solution of adrenalin hydrochloride (1 to 1000). The writer is without experience with the method, but would regard injections as adding an unnecessary danger of infection.

*Repetition of Tapping.*—One tapping suffices in about 75 per cent. of the cases. In about 20 per cent. of the remaining cases there is no more fluid after the second operation. In some cases evacuation must be frequently repeated. It is often difficult to determine the presence of fluid in cases which have been tapped, owing to the changes in the pleura. Percussion often gives dubious results and more reliance may be placed on the absence of tactile fremitus, the respiratory murmur, and cardiac displacement.

*Dangers of Thoracentesis.*—There is some danger in the performance of thoracentesis. This is reduced to a minimum by the strictest asepsis, the use of an air-tight trocar, rather than an ordinary needle, the slow withdrawal of only moderate amounts of fluid without forcible aspiration, and a careful selection of cases. Unavoidable accidents are extremely rare. Patients are more often sacrificed by hesitation and delay than by its use.

If performed with an imperfect technique, a serous may be converted into a purulent effusion. Of 553 tappings in the writer's series, turbid fluids were found in 27, and of these 12 later became purulent, but the suppuration was probably spontaneous. In one instance a fluid showed 88 per cent. of lymphocytes at the first tapping and 78 per cent. polynuclear cells when the thoracentesis was repeated four days later. In a second case a fluid at first contained 96 per cent. lymphocytes. The patient was discharged without evidence of effusion, to return one month later with empyema. Whether a similar change would have taken place without puncture is uncertain.

Capps and Lewis[2] have recently shown that a mechanical irritation of an inflamed pleura, experimentally produced in animals, frequently gives rise to a reflex, of a vasomotor type, which lowers the blood pressure and may cause death. The most efficient remedy for this form of shock is the intravenous injection of adrenalin.

[1] *British Medical Journal*, 1904, p. 1003.
[2] *Transactions of Association of American Physicians*, 1907.

*Pneumothorax* is a more frequent result. In rare instances it may be due to puncture of the lung or to the rupture of adhesions, pulmonary cavities, or emphysematous blebs during expansion. It is not infrequently due to the entrance of air through an unguarded needle or trocar, as Sears[1] has recently emphasized. It may also result from accidental inflation of the pleural sac with the aspirating pump, if the tubing is misapplied. Infection of the pleura may follow the admission of air.

Subcutaneous emphysema may occur if the lung is wounded and air enters the track of the needle or trocar. It may be local or involve the greater part of the body, and is more common after exploratory puncture. Extension of malignant growth or tubercle along the track of the needle occasionally occurs. The removal of pleural fluid may lead to the detachment of thrombi in the heart or intrathoracic vessels, with monoplegia or hemiplegia as a result. Delirium and hysterical and epileptic attacks have been observed. Urticaria has been noted after thoracentesis, and should always suggest echinococcus disease.

*Albuminous expectoration* is of rare occurrence. Terillon[2] collected 21 cases. Riesman[3] has recently reviewed the literature and reported an additional instance. Osler observed the condition twice in 195 cases. It occurred once in the writer's series. The albuminous expectoration usually begins during or shortly after the withdrawal of fluid. Its appearance may, however, be delayed for as long as eighteen hours, as in Pepper's case. It is accompanied by cough and often by dyspnœa, which varies much in intensity and may be extreme, with cyanosis and rapid, feeble pulse. Rales may be heard over the lung during the attack. Its duration and intensity are very variable. It may last for as long as forty-eight hours, and the patient may die of suffocation. The fluid may amount to as much as a quart in two hours, but smaller quantities are more common. The expectorated fluid is serous and contains a variable amount of blood, frothy mucus, and albumin. In most instances an excessive amount of fluid (more than 2000 cc.) has been removed. The condition has been more often noted in acute effusions, but Riesman's case was chronic. In the case in the writer's series only 1000 cc. of fluid were withdrawn. The expectoration began a few minutes after the tapping, and lasted for four hours, during which time about 500 cc. were expectorated. The pulmonary symptoms completely subsided, but the patient died some weeks later, and at autopsy cirrhosis of the liver and associated lesions were found, but no explanation of the expectoration. In fatal cases œdema of one or both lungs, cardiac disease, fibrinous plugs in the bronchi, and adherent pericardium have been found (Riesman). The condition has been ascribed to evacuation of pleural fluid by way of the bronchi. This may happen if the lung has been perforated during the puncture. Spontaneous rupture or filtration through the lung has been suggested. It is more probably due, however, to pulmonary congestion, with œdema, for which Riesman suggests the term "congestion by recoil." It may be conjectured that compression of the lung is followed by changes in its bloodvessels, and that in the congestion after re-expansion there is a transudation of serum.

Death, in rare instances, has followed even simple exploratory puncture.

[1] *American Journal of the Medical Sciences*, December, 1906, p. 850
[2] *L'expectoration albumineuse, Thèse de Paris*, 1873.
[3] *American Journal of the Medical Sciences*, 1902.

Sears collected 10 cases from the literature and reported an additional instance; 7 were in children and in 8 solidified lung had been punctured. Irritation of the pulmonary terminations of the vagus or hemorrhage into the pleural cavity from a wound of the lung have been suggested in explanation. Artificial pneumothorax has occasionally been fatal. Sudden death during or after the evacuation of pleural fluid may be due to embolism. Thrombi in the pulmonary veins or the venæ cavæ are the most frequent source. Syncope and death may occasionally be due to cerebral anæmia, from afflux of blood to the re-expanded lung. Fatal hæmoptysis has followed the wounding of vascular granulation tissue in the lung or of blood-vessels lining the walls or traversing the lumen of pulmonary cavities. Such vessels may be also ruptured during expansion of the lung. Perforation of the diaphragm has been followed by fatal peritonitis or hemorrhage from the spleen. Miliary tuberculosis may, in rare instances, arise from infected thrombi set free from pulmonary vessels by the evacuation of tuberculous fluid (Fränkel). If the lung is adherent, fatal hemorrhage from pleural vessels may follow forcible aspiration. Injury of an atheromatous intercostal artery has been followed by fatal bleeding (Naunyn).

*Results of Thoracentesis.*—Following the removal of fluid, there is usually a marked improvement in the breathing and cardiac action. The patient's color is better and there may be an increase in the amount of urine. The heart returns to its normal position unless prevented by adhesions or marked indurative processes. The temperature may fall at once, but gradual defervescence is more frequent. The duration and intensity of the pleuritis appear to be lessened. Re-expansion of the lung is more rapid, absorption of the remaining fluid takes place, and subsequent deformity with contraction of the side, narrowing of the intercostal spaces, and displacement of diaphragm and heart are less frequent. It is a mistake to regard such patients as cured, however, for too often the subsequent history shows that the pleural symptoms have been relieved, but that an underlying tuberculous process continues to extend.

In some cases thoracentesis is actually life saving. This applies more often to the cases in which early diagnosis of the tuberculous process puts both patient and physician in possession of evidence without which only half measures would have been carried out in further treatment. It also applies to cases with alarming pressure symptoms in which evacuation of fluid is immediately life saving.

(*a*) *After-treatment.*—The operation of thoracentesis affects the general management of the case very little. If the patient has been in the reclining position, following the operation, a bed-rest may first be given, then a change from the bed to a chair, and the patient may be up and about by the end of the week, provided no contra-indications are present. This interval of quiet is wise even if all goes well, to allow time for readjustment to the changed intrathoracic conditions and repair in the inflamed pleura.

(*b*) *Respiratory Exercises.*—Their purpose is to favor expansion of the lung on the affected side and to prevent contraction of the chest with limitation of the breathing capacity. The presence of fever, pain, accumulating fluid, or active pulmonary disease may be regarded as contra-indications. Despite the theoretical value which respiratory movement is thought to have on absorption, it seems unwise to begin exercise before the end of the second week after thoracentesis, the indication meanwhile being to rest

the inflamed tissue, as in similar processes elsewhere. Gymnastics should even then be cautiously begun, being guided by the symptoms which follow. Pain during the procedures may be taken to indicate tension on pleural adhesions and too vigorous exercise may rupture the lung.

Forced inspiration from six to twelve times every two hours may serve as a beginning. Later, with each inspiration, the outstretched arm on the diseased side may be elevated to a horizontal, then to a vertical position, with coincident compression of the sound side by the other arm. Lateral deviation of the spine toward the sound side during inspiration more forcibly puts the diseased side on the stretch. It may be combined with a similar movement, holding both arms outstretched at right angles with the body. This, as well as torsion of the trunk with the arms similarly placed, should, however, be preceded by simpler exercises and practised only late in the course. Wolff's bottles, the contents of which the patient blows alternately from one to the other, furnish a simple and helpful respiratory exercise. An arm-chair may be used, as suggested by Naunyn. The patient sits with the sound side compressed against the arm of the chair, maintaining this position by a tight grasp of one of the rungs of the chair with the corresponding hand. In this position inspiratory efforts are largely spent in the expansion of the affected side. Valuable respiratory exercises may be combined with the use of the Zander apparatus. Fränkel suggests the inhalation of compressed air, beginning with one one-hundredth and gradually increasing to one-sixtieth of an atmosphere. Aron[1] recommends the pneumatic cabinet.

(*c*) *Elimination.*—Efforts to eliminate pleural fluid by the bowel (calomel, saline, and hydragogue cathartics), through the skin (hot packs, hot-air or vapor baths, pilocarpine), or kidney (diuretin, digitalis) have long been used, but are uncertain, and from their depressing effect may do more harm than good. The thirst cure, in which the ingestion of liquids is restricted to a minimum, is not to be recommended. The chloride reduction cure for pleural effusions has as yet been little used. Chauffard and Boidin[2] recommend a milk diet from its low content of salt.

(*d*) *Drugs.*—There are no drugs with any specific action on the disease. Sodium salicylate, when pleuritis complicates acute articular rheumatism, or is due to a similar cause, is recommended by many. It may quiet pain. The writer does not believe that it is a specific either for rheumatism or pleuritis. The use of morphine is most valuable for pain.

(*e*) *Tuberculin.*—This may be of service in connection with hygienic and dietetic treatment of tuberculous cases. If used, it should be given as in pulmonary tuberculosis, to the section on which the reader is referred.

(*f*) *Thoracotomy.*—In rare instances the rapid accumulation of serofibrinous fluid (pleuritis acutissima) of a gelatinous consistence from abundant fibrin may prevent evacuation by means of the trocar. Thoracotomy may then be considered as a life-saving measure.

## Acute Purulent Pleuritis.

**Etiology.**—Certain differences between the etiology of this and other forms of pleuritis may be mentioned.

[1] *Therapeutische Monatsch.*, 1896, x, p. 473.
[2] *Gaz. des hôpitaux*, 1904, No. 51.

**Primary Form.**—The proportion of cases in which empyema is apparently primary is relatively small compared with fibrinous and serofibrinous pleuritis. Of 252 cases with empyema in the writer's series, 83 (32.9 per cent.) may be classed in this group against 64 and 63 per cent. respectively for the fibrinous and serofibrinous form. Primary empyema is said to be more common in children, but expectoration is often absent and an effusion may make the detection of a pulmonary process difficult or impossible.

**Secondary Form.**—As in other varieties of pleuritis, disease of the lung occupies first place and can be demonstrated in a larger proportion of cases, since the pulmonary lesions leading to suppuration in the pleural sac are more easily detected. Thus, of 252 cases in this series, 158 (62.6 per cent.) appeared to be pulmonary in origin, including 140 cases of pneumonia (136 lobar pneumonia, 4 bronchopneumonia), 15 of pulmonary tuberculosis and 3 of abscess or gangrene of the lung. Gangrene leads to putrid exudates. The disease may arise by extension from the abdomen, the pericardium, or the other pleura; it may complicate the infectious diseases (influenza, typhoid fever, etc.) or suppurative lesions in any part of the body, as has been mentioned for the other forms of pleuritis. It may be caused by trauma and may follow the serofibrinous form.

In children empyema is, in general, more frequent than serofibrinous effusion. There is, however, considerable variation in statistics on this point. Of 169 cases under ten at St. Bartholomew's Hospital analyzed by Gee, 84 were non-purulent, 85 purulent. The younger the child, the more likely is the exudate to be pus. Thus, of Gee's 78 cases under five, 53 were purulent. Of 116 cases under five in Carpenter's series, 77 were empyema. In adults, on the contrary, serofibrinous effusions are much more common.

1. **Pneumococcus.**—This appears to be the most frequent organism occurring as a pure infection. Of 109 empyemas investigated by Netter, it was present in 53.6 per cent. of 28 cases in children, while in 81 cases of adults it was found in 17.3 per cent. Of 137 cases in the writer's series, the pneumococcus was found in 54 (39.4 per cent.). It is the most common cause of metapneumonic effusions, but may also be found in primary empyema. The organism shows a marked tendency to die out. It may be found in smears from the pus, but cultures from the same fluid are not infrequently sterile. To this is probably due the relatively favorable course of pneumococcus empyema. It is probable that it is the cause of suppuration in tuberculous empyema, in which tubercle bacilli may be found on inoculation, but cultures are sterile from the disappearance of the pneumococcus.

2. **Streptococcus.**—Netter found this in 51 cases (46.7 per cent.). It was present in 28 (20.4 per cent.) of the writer's cases. Serofibrinous effusions containing streptococci are likely to become purulent.

3. **Tubercle Bacilli.**—This has not been shown to be as frequent a cause of purulent as of serofibrinous effusions. Of Netter's 109 cases, 12 were found to be tuberculous. The finding of other organisms does not exclude the tubercle bacillus nor does the presence of the tubercle bacillus alone exclude other organisms such as the pneumococcus, which may have died out.

4. **Staphylococcus.**—This is relatively infrequent. It was present in only one of Netter's cases. In the writer's series it occurred in 5 (3.6 per cent.).

5. **Mixed Infections, etc.**—Infection with more than one organism was found in 22 (16 per cent.). The pus may be sterile, as in 25 cases (18.2 per cent.), and infection with the tubercle bacillus or the pneumococcus

may be suspected. Other organisms than those already mentioned are uncommon. Influenza bacilli, typhoid bacilli, *Bacillus mucosus capsulatus*, *Streptococcus capsulatus*, diphtheria bacillus, colon bacillus, actinomyces, etc., have been found. Mixed infections are constant with putrid exudates.

**Types of the Disease.**—The purulent pleurisies have been separated into different groups according to their bacterial etiology. Mixed infections with one or more organisms are common, and the tubercle bacillus may co-exist, but elude detection. Sterile exudates are difficult to place; they are usually due to the tubercle bacillus, rarely to the pneumococcus. It seems to the writer that as yet no distinctive clinical picture can be formulated for the various forms, and that with few exceptions the clinical and pathological similarity of the different infections is more striking than their dissimilarity. It still seems best to consider the various infections together and refer to such differences as can be noted under the separate headings.

**Special Pathology.**—The pleura is the site of a fibrinous or fibropurulent layer. It is grayish white or yellowish in color, and may be greatly thickened. The inflammation may be general or circumscribed. The sacculation of fluid is not infrequent. Erosion, ulceration, or even perforation of the visceral or parietal pleura may be found. These destructive processes may be single, but are more commonly multiple and limited to the pulmonary layer. After long-standing empyema, allowed to run its course untreated, calcification and the formation of bony plates may take place in rare instances.

In fatal cases other organs are seldom uninvolved. The lung is the most frequent site of changes, from which the pleural disease has usually arisen secondarily. Lobar pneumonia, bronchopneumonia, abscess, and gangrene may be the source of the process. After long-standing empyema, chronic interstitial changes may occur about the lung and penetrate the pulmonary tissue along the interlobar septa, the so-called pleurogenous interstitial pneumonia. Suppurative pulmonary lesions and bronchiectasis are likely to co-exist. It is often difficult to tell whether the lung is primarily or secondarily invaded. In some instances, pleural suppuration extends to the pericardium, peritoneum, or the mediastinum, from which the opposite pleura may become infected. Endocarditis is not uncommon. The spleen may be large and soft. Thrombosis of intrathoracic or other vessels may be present. Cerebral abscesses may occur. Tuberculosis of the pleura, lungs, or bronchial glands was present in 9 of 38 cases at autopsy in the writer's series. Tuberculous lesions in more remote parts of the body were found in 2. Thus, about 30 per cent. showed tuberculosis in some part of the body.

**Location.**—Of 248 cases in the writer's series, the right side was affected in 122, the left in 121, and both in 5. Purulent are more often encapsulated than serofibrinous fluids. Encapsulation was discovered in 8 of the present series. When empyema complicates pneumonia, the effusion is usually at the bases irrespective of the site of the pneumonic process.

**The Effusion.**—No sharp dividing line can be drawn in gross appearance between serofibrinous and purulent fluids. The fluid may be merely turbid, with a few fibrinous flocculi and contain an excess of polynuclear cells on microscopic examination. It must be remembered that pus may sediment

within as well as outside the chest. At operation or autopsy tolerably clear serum may be found above with a layer of pus at the bottom of the pleural sac. The effusion may be serofibrinous at first and become purulent later. There is often, however, an excess of polynuclear cells in such fluids from the beginning. In color the fluids may be yellowish, with varying shades of greenish. They may be reddish or even frankly red, brownish or chocolate colored from the presence of blood. With large amounts of pus they are grayish, greenish-yellow, or cream colored. They may be without odor, sweetish, or fœtid. In gangrene of the lung or pleura they often have a horribly offensive odor. The specific gravity is higher than in serofibrinous fluids. It may reach 1030 or more. The amount of solids is often 60 to 70, but may reach 90 to 100 p. m. (Hammersten).

**Symptoms.**—These are usually the same as are seen in the serofibrinous form and certain differences only need be mentioned. They are not distinctive of empyema. The onset is likely to be more acute. An insidious onset and latent course are less common than in the serofibrinous form. Toxic symptoms are more common and more severe. In general, the temperature is higher; of 145 cases in the writer's series, only 2 ran an afebrile course. From 101° to 103° is an average pyrexia, but the temperature reaches 104°, 105°, or even higher in a larger proportion of cases, with wider variation between the morning and evening elevations. The respiration and pulse are likely to be more rapid. Recurring chilliness or chills, a more rapid loss of strength and weight and increasing pallor may be mentioned. Between the various infections there are no constant differences. Pneumococcus empyema may be relatively mild. Streptococcus infections are more severe, and putrid exudates are accompanied by most marked disturbances. In the latter, bad taste in the mouth, foul breath, and foul sputum may be present. Uncomplicated tuberculous effusions may run an afebrile and long course without marked general symptoms. In rare instances empyema may persist without symptoms for months or years. In Faisans and Audistère's case the disease may have lasted for forty years. At autopsy there was sterile fluid contained in a space, the walls of which were transformed into cartilaginous and osseous tissue.

**Physical Signs.**—These are such as have been considered under Serofibrinous Effusion. The affected side may be more prominent, with wider intercostal spaces which may actually bulge. Œdema of the chest wall is uncommon, but more frequent with purulent than with serous fluid. The subcutaneous veins may be dilated. Whispered pectoriloquy (Bacelli's sign) has proven an uncertain differentiation from serofibrinous pleuritis in the writer's experience. A disproportion between the amount of fluid and the severity of the symptoms may be suggestive. The displacement of the heart and the liver are relatively greater with purulent than serofibrinous fluid, due probably, as Senator has suggested, to the greater weight of the former. In children the breath sounds may be loud and bronchial over a purulent effusion. The axillary glands are occasionally enlarged on the affected side, as in 2 of the 145 cases in the writer's series. In 1, suppuration was present. The spleen may be enlarged. In long-standing cases, especially in children, clubbing of the fingers may occur.

**Pulsating Empyema.**—This condition is more commonly associated with suppuration in or about the pleural sac. Of 95 cases analyzed by Sailer[1]

[1] *American Journal of the Medical Sciences*, 1904.

there was pus in the pleural sac in 71, and of these there was tumor (empyema necessitatis) in 38. In 13 there was intrapleural or extrapleural abscess. The remaining cases were non-purulent or their condition was not definitely known. The condition appears to be more common in males and in early life. Pulsations may be diffuse or localized, single or multiple, and are often seen on the left side. They are most common in the parasternal regions, but may occur in the lower lateral and posterior parts of the chest. Pulsation is probably due to an accumulation under pressure of fluid which is apposed to a lung made inelastic by collapse or pathological changes in or about it, and to some local or general weakness of the thoracic wall.

**The Blood.—White Cells.**—In 28 cases of primary empyema the white count was above 12,000 in all but 6, *i. e.*, between 12,000 and 16,000 in 3; 16,000 to 20,000 in 7; 20,000 to 24,000 in 4; 26,000 to 35,000 in 3, and 35,000 to 50,000 in 5. The 6 cases with a low white count recovered after operation. No conclusion can be drawn from the white count in this small number of cases concerning the prognosis or the character of the infecting organism. The white count may, however, be of great value in distinguishing uncomplicated tuberculous serofibrinous effusion from empyema, only 3 of 33 cases with the former showing a white count above 12,000.

**Complications.**—These are much the same as for serofibrinous pleuritis.

1. **Extension to Neighboring Organs.**—This is more common in empyema. (*a*) *Perforation of the Lung.*—This may be *latent* and indicated only by the expectoration of muco-purulent sputum. Evacuation of small amounts of pleural pus by this means is frequent. The complication is frequently overlooked and pneumothorax does not occur. In other cases the perforation is *obvious*. In this form pneumothorax is more common, but does not necessarily occur. In some instances there is a sudden paroxysm of cough, with the evacuation of a large amount of pus. If perforation occurs while the patient is asleep or if the lung is suddenly flooded, death may take place from suffocation. Single or multiple fistulous tracts may connect the pleura with the bronchi, and pneumothorax may thus arise. Invasion of the lung usually leads to multiple abscesses connecting with the bronchi. In some instances the affected lung may present a honeycombed appearance. Single pulmonary abscesses are less common. It is difficult to tell in individual cases at autopsy whether the lung has been primarily or secondarily involved. Of 11 cases with pulmonary suppuration and empyema at autopsy in the writer's series, abscesses were multiple in 8, single in 3. Pulmonary gangrene may occur, but is less common. Chronic interstitial pulmonary changes are likely to follow if the patient recovers. Perforation of the lung was absent in 41 cases of pneumococcus empyema in the writer's series; present in 2 of 19 streptococcus cases. It is a serious event. Of 145 cases obvious perforation occurred in 5. One patient recovered. A second has persistent cough, with abundant purulent sputum and frequent attacks of hæmoptysis, but is otherwise well now, six years after the perforation. The 3 remaining patients died, 1 from suffocation, the others from sepsis. Evacuation by the lung does not obviate the necessity of thoracotomy, which should be done to spare the lung from further damage. Pulmonary perforation may occur at any time, but is uncommon before the third or fourth week.

(*b*) *Perforation of the Thoracic Wall* (*Empyema Necessitatis*).—This is less common than pulmonary perforation. It is more favorable and may be followed by complete evacuation and recovery. The abscess may point in any part of the chest, but perforation is more often seen in the parasternal region or in the fifth interspace outside the nipple line, the thinnest regions of the chest. The perforation may be single or multiple. It seldom occurs before the end of the first month, but may take place at any time after this period. The abscess usually forms an irreducible fluctuating tumor, becoming more tense with forced expiration or cough. It is dull or flat on percussion. In a case observed by the writer, a reducible resonant tumor was present in the left second interchondral space, shown by operation to be due to pyopneumothorax. The opening into the thorax may be at some distance from the site of the tumor, the rupture of which may be followed by discharge of a relatively large amount of fluid. Forced expiration and cough may hasten, inspiration may diminish the flow. The tumor may pulsate. Evacuation by spontaneous perforation is usually incomplete. The fistula is likely to close, the pleural pus to re-accumulate, with subsequent perforation in the same or other places. Cure by this means is rare and thoracotomy is indicated. Caries of the ribs and necrosis of the soft parts may arise from the perforation. Erosion of an intercostal artery may lead to fatal hemorrhage. Perforation is more common in streptococcus, tuberculous, mixed, or putrid infections. Actinomycosis should always be considered in the presence of abscesses of the chest wall arising by extension from within. Simple thoracic abscesses may be unaccompanied by pulmonary or pleural changes and are uninfluenced by changes in intrathoracic pressure. The distinction may, however, be impossible before exploration by operation. Suppuration in the tissue between costal pleura and thoracic wall (peripleuritis) leading to external perforation, may simulate encapsulated empyema necessitatis.

(*c*) *Perforation of the Diaphragm.*—This is more serious. It may lead to local or general peritonitis. As in perforation of the lung, it is often difficult in individual cases to tell whether the infection has spread from the pleura to peritoneum or in the opposite direction. Obvious gross lesion of the tissue may be absent. In other cases the site of the perforation may be readily found. Peritonitis was present in 9 of 38 autopsies on cases of empyema in the writer's series. It was general in 7, localized in 2. Streptococci were present in 7, either alone or mixed with other organisms. In one of the writer's series an encapsulated diaphragmatic empyema pointed in the right hypochondrium; recovery followed operation. In a case of pneumococcus empyema and general pneumococcus peritonitis seen with C. L. Scudder, recovery followed repeated abdominal operations and costatectomy. An abdominal abscess, starting from the pleura, may perforate the stomach, the intestines, or the kidney. It may extend along the spine to the iliac fossa and simulate psoas or lumbar abscess.

(*d*) *The œsophagus may be perforated*, as in the cases reported by Voelcker, Thursfield, and Osler, with the formation of pleuro-œsophageal fistulæ.

(*e*) *Infection of the pericardium* is probably more often present than statistics show. It was recognized during life in 4 of 145 cases, but was present at autopsy in 6 of 38. Inflammation may also extend to the mediastinum.

2. **Metastatic Lesions.**—It is uncertain in individual cases whether suppurative lesions in remote parts of the body are primary or secondary. They may arise by extension of the pleural infection to the intrathoracic veins or the endocardium. From an infected thrombus thus formed, emboli may be carried to the brain, kidney, spleen, or other organs, with the production of infarct or abscess. Cerebral abscesses are among the most dangerous complications, and are usually multiple, as in 3 of 38 autopsies in this series. Pulmonary abscesses were associated in 2. In 1 the cerebral abscesses were unaccompanied by suppurative foci elsewhere than in the pleura. Septicæmia is a common occurrence in empyema.

3. **Amyloid Degeneration** may complicate long-continued suppuration.

**Causes of Death.**—The same danger of sudden death and similar causes obtain in purulent as in serofibrinous effusion. These need not be further considered here. It is uncommon in fatal cases not to find suppurative processes in neighboring or other parts of the body. Peritonitis is one of the most frequent of coincident infections, and was present in 9 of 38 fatal cases in the writer's series, but the complicated character of fatal cases makes it difficult to judge between immediate and contributing causes of death. Pneumonia, pulmonary abscess and gangrene, pericarditis, endocarditis, thrombosis of intrathoracic veins or the auricles, with or without infarction, cerebral abscesses, and meningitis, may be regarded as important factors, either singly or combined. The streptococcus is the most frequent organism, but pneumococci are often present and other organisms may be found.

**Relapse.**—The recurrence of empyema in the same place after complete recovery does not occur, because of the obliteration of the pleural sac at this place. Incomplete absorption or removal may, however, be followed by a return of symptoms and an increase in the amount of fluid. Incomplete evacuation, insufficient drainage, encapsulation, the presence of undiscovered pockets of pus or the development of empyema elsewhere may be responsible for a second accumulation of fluid.

**Sequelæ.**—It is rare, on physical examination of patients who have recovered from empyema, not to find signs of the previous disease. There is diminished expansion of the affected side, which often looks smaller, and measurement shows that it is contracted. The interspaces are relatively narrow. Toward the base there is slight relative dulness, its upper limit often being highest behind and extending in a nearly horizontal line toward the axilla, where it gradually descends to the inferior pulmonary margin in the anterolateral thoracic region. The extent of dulness is variable and may involve half of the chest. The tactile fremitus may be diminished over the dull area. The breathing, voice sounds, and whisper may be diminished, but are often unchanged. In cases which have run a long course before evacuation takes place, with abundant connective-tissue formation about the lung or within its substance, the lung may be partially or wholly incapable of re-expansion. A space is left which is filled by fibrous tissue, by the collapse of the chest wall, the dislocation of the mediastinum and heart toward the affected side, the displacement upward of the diaphragm and partial expansion of the lung, depending on the changes which have taken place in and about it. In rare cases, with dulness, there may be signs suggestive of slight degrees of pulmonary solidification. These may be due to interstitial changes in the lung, or, if marked retraction has taken place,

to proximity of the larger bronchi to the chest wall. In the young, with less resistant thoracic walls, marked deformity with retraction of the side, drooping of the shoulder and lateral deviation of the spine may result.

Pain of variable and usually slight intensity may persist in the affected side. Of 26 patients investigated on this point in the writer's series, 8 still have pain for periods of one to seven years after discharge.

**Diagnosis.**—The diseases with which pleural effusion may be confused, the differentiation of pleural fluids of different character, the method of employing exploratory puncture and the examination of pleural fluids have already been discussed under Serofibrinous Pleuritis and may be applied also to empyema. Certain additional features in the diagnosis of empyema may, however, be emphasized with special reference to exploratory puncture, exploratory incision, and the examination of purulent fluid.

**Exploratory Puncture.**—This is indicated if pus is suspected. By hesitation and delay, the disease may be converted into a chronic and incurable affection. In acute cases, with typical signs of fluid, it is practically devoid of danger, and, if present, pus can usually be demonstrated by this means. In some cases, however, it is missed by the trocar or is too viscid to flow; a negative puncture does not exclude pus.

*Cases in which Exploratory Puncture is Dangerous.*—In cases of empyema of long standing, in which there is contraction of the side, elevation of the diaphragm, and secondary suppurative lesions in the lung, or in cases in which empyema complicates pulmonary abscess, gangrene, bronchiectasis, and interstitial pneumonia, the conditions are less favorable for exploratory puncture. The pleural pus is often small in amount, and may be encapsulated between lung and diaphragm or in other parts of the chest. The diagnosis of pleural involvement in the cases under consideration can usually be made. The history may afford important evidence. Lobar pneumonia and infection of the thorax from without never spare the pleura. There may be a history of pain characteristic of pleural invasion or of symptoms consistent with the rupture of empyema into the lung. The physical signs may be atypical, but if the pus reaches the chest wall, localized tenderness, dulness or flatness on the affected side and the opposite paravertebral region, diminished or absent breathing and voice sounds, with œgophony, and the absence of tactile fremitus, whispered pectoriloquy and the diaphragm shadow may disclose the presence of an effusion. It is well to confirm the results of physical examination by radioscopy. Exploratory puncture is not without danger in cases thus complicated. Bloodvessels lining the walls or traversing the lumen of pulmonary cavities or fresh granulation tissue, if injured by the trocar, have been the source of fatal hemorrhage. Perforation of the elevated diaphragm has caused fatal peritonitis. In the presence of such complications, with typical signs of fluid and displacement of the heart, exploratory puncture may be made, but with care not to introduce the instrument too far or through the diaphragm, the position of which should be determined by *x*-ray examination. In similarly complicated cases, in which from the history, the physical signs, and the *x*-ray examination there is good reason to suspect pus, the demonstration of which with the trocar has failed or cannot be safely undertaken, it is better to resort to exploratory incision.

**Exploratory Incision.**—This is indicated, as already mentioned, when there is good reason to suspect pus which cannot be demonstrated by exploratory

puncture or in complicated cases in which it is a less dangerous procedure. It should be entrusted only to an experienced surgeon. The writer has advised exploratory operation without previous exploratory puncture in cases such as have been described above, and has not seen an unfavorable result. The technique of operation cannot be considered here. The chief danger is artificial pneumothorax, which may arise if the lung is free. Incision and costatectomy, with care not to wound the pleura, will disclose the condition of the underlying tissue.

**Examination of Pleural Pus.**—Fluids on the border line between the serofibrinous and purulent variety may be examined as already indicated in the preceding section. Cultures should always be made. With frank pus, tubercle bacilli may be demonstrated by the following means: A few cubic centimeters are transferred to a flask and diluted with 10 volumes of water. A few drops of strong alkali (KOH or NaOH) are added and the solution is gently heated. After the cellular elements are dissolved, the solution may be centrifugalized and the precipitate investigated for tubercle bacilli. Animals cannot be inoculated with large amounts of pus or intraperitoneally without a too rapidly fatal termination for the demonstration of tuberculosis. It is best, therefore, to inject only 1 to 2 cc. of pus under the skin.

**Prognosis.**—Absorption of empyema rarely, if ever, occurs. Spontaneous disappearance of pus has been noted in isolated cases by Fürbringer, Gerhardt, Fränkel, Schede, and others. It may be due, as Curschmann suggests, to latent perforation of the bronchi. Recovery may follow obvious perforation of the lung, but usually with most distressing and dangerous complications. After perforation of the chest wall recovery may follow. Most cases, if untreated, end in death. Of 252 cases in the writer's series 56 (22.2 per cent.) died in hospital.

**Treatment.**—In general, pleural pus should be evacuated as soon as the diagnosis is made. *Constant, free drainage is essential for prompt and permanent cure.* Various methods may be briefly considered, but for more detailed information works on surgery must be consulted.

1. **Thoracotomy with Costatectomy.**—This is the operation of choice. The incision is best made in a dependent part of the pleural cavity, with resection of the seventh or eighth rib in the posterior axillary line. Pus should be evacuated slowly. Irrigation of the cavity is seldom necessary and may be dangerous. With empyema necessitatis, enlargement of the perforation in the chest wall may suffice if this is in a favorable position for drainage. Otherwise, a second opening in a more suitable position should be made. If the pus is encapsulated, the incision must be made where drainage will be most effective. Thoracotomy alone often affords insufficient drainage and costatectomy is often necessary later.

2. **Other Methods.**—These are less efficient since drainage is often neither constant nor free, but they may be used in selected cases, as a preliminary to the radical operation or as palliative procedures.

(*a*) *Thoracentesis.*—This may be considered for effusions on the border line between the serofibrinous and purulent forms. It is indicated for the evacuation of an exudate of large size, with or without pressure symptoms, as a life-saving measure or a preliminary to operation, thus avoiding the danger of more rapid evacuation, and as a palliative procedure in empyema complicating advanced pulmonary tuberculosis. Although repeated puncture has been advised for pneumococcus empyema, especially in

children, it is uncertain, likely to be followed by re-accumulation, and leads to complications and greater deformity of the chest. It frequently delays operation, which is often necessary later, and subjects the patient to an unjustifiable risk.

(*b*) *Siphon Drainage* (*Bülau*).—By this method[1] drainage is afforded, but evacuation is often neither constant nor free. Slow evacuation, avoidance of narcosis, and a large operation wound, no danger of pneumothorax, and better expansion of the retracted lung are advantages claimed for the method. The apparatus requires constant attention, pus is less likely to be completely evacuated, and masses of fibrin may readily obstruct the tube. Fluid may escape or air enter about the tube. It is, therefore, more suitable for hospital patients or where constant attention is possible. It may be tried at the extremes of age, in weak patients unable to stand the radical operation, in relatively benign pneumococcus empyema, without much fibrin, and in double empyema, in which collapse of the lung from pneumothorax is to be avoided.

**Tuberculous Empyema.**—In this form the indications are less clear and considerable difference of opinion exists concerning the appropriate treatment. In an advanced stage of the disease a radical operation can hardly be considered, and such palliative measures as repeated puncture or siphon drainage may be tried. The decision is more difficult when empyema complicates early pulmonary tuberculosis. Bäumler[2] considers that the presence of pyogenic cocci in the exudate demands thoracotomy and best combined with costatectomy, that with tubercle bacilli alone or sterile exudates and pressure symptoms, aspiration may be tried, and if the lung is found capable of expansion, if not too much invaded and the other lung is tolerably free, thoracotomy may be done after some improvement in the general condition. Of 31 cases of tuberculous empyema operated by Küster, 9 recovered, 6 were not cured, and 16 died. In Schede's collective investigation of 45 cases, 10 were cured and 35 died, a mortality of 77 per cent. In general, tuberculous empyema is the most unfavorable form. Of 12 cases, with sterile exudates, in the writer's series, only 1 of whom showed tubercle bacilli in the sputum, 3 died in hospital. Of the remaining 9 patients, 6 have been traced. All have died except 1, who has a discharging sinus, now seven years after operation, but is otherwise well. Sterile exudates are usually, but not necessarily, tuberculous, and in this patient, in whom the empyema was metapneumonic, the process was probably due to the pneumococcus.

**After-treatment.**—Expansion of the lung may be favored by various devices, permitting the outflow of pus and air through the drainage tubes during expiration, but preventing the re-entry of air during inspiration. A thin layer of impervious material (mackintosh, protective silk) may be applied over the opening of the tubes. The dressing itself, when soaked with secretion, may suffice. A vacuum apparatus may be used as in Perthes' method. After closure of the sinus, respiratory exercises are valuable. Throughout the illness, every means should be taken to build up the general health.

[1] A trocar 6 to 7 mm. in diameter and armed with a stop-cock is inserted through the seventh or eighth axillary space. Through this a rubber catheter is passed and the trocar withdrawn. One end of a short piece of glass tubing is inserted into the free end of the catheter, the other into a rubber tube, leading to a receptacle, attached to the bed or placed on the floor.

[2] *Deut. med. Woch.*, 1894, Nrs. 37 und 38.

**Vaccination.**—The subcutaneous inoculation of vaccines, according to Wright's method, may be considered in the absence of auto-inoculation and for the treatment of a persistent sinus. Their value must be left for the future to decide. According to present indications and the writer's experience, the control of the dosage by the opsonic index is unreliable.

**Results of Operation.**—The mortality of the operation itself is very low. In patients already near the end, it may hasten the fatal termination, but even in the most desperate cases, evacuation by some means is justifiable.

1. *Immediate Results.*—The success or failure of operation is largely dependent on the period at which the disease is discovered, the character of the underlying process, and the infecting organisms. Too much reliance, however, cannot be placed on these factors in individual cases. In general, the results are much more favorable when the empyema is detected early. Concerning the character of the underlying disease, tuberculous cases are most unfavorable. Of 45 operations on tuberculous empyema in Schede's collected cases, there was a mortality of 77 per cent. and an average duration of 136 days from operation to recovery in favorable cases. Judging from Schede's cases, secondary and metastatic empyema stands next in the number of fatalities, with a mortality of 32 per cent. in 50 cases. Of 288 metapneumonic empyemas, the mortality was 13 per cent., with an average of 83 days for recovery, while idiopathic empyema was most favorable with a mortality of 7.9 per cent. among 101 cases and 66 days for recovery. In regard to the relation between the immediate results and the infecting organisms, the duration of the process, the character of the underlying disease, the presence of complications and various other factors must be considered. Large series of cases are lacking. To judge from the small series collected by the writer, excluding obviously tuberculous cases, the mixed infections seem to be most unfavorable. Of 27 cases in this group (mostly pneumococcus and streptococcus, and including 8 primary, 18 metapneumonic, and 1 with abscess of the lung), 5 (18.5 per cent.) died in hospital. Of the fatal cases, 1 was primary, the others metapneumonic. The pneumococcus cases appear to stand next in the number of fatalities, for of 35 cases (including 6 primary, 26 metapneumonic, 2 following trauma, and 1 complicating measles), only 4 (11.4 per cent.) died in hospital. Of the fatal cases, 1 was primary, 3 were metapneumonic. The mortality of the streptococcus cases was even lower. Of 17 pure streptococcus infections (8 primary, 9 metapneumonic), only 1 (5.8 per cent.) metapneumonic case died in hospital. Streptococcus cases are usually considered especially unfavorable. Judging the severity of the different infections by the average stay in hospital from operation to discharge,[1] there is no striking difference between the different groups. For the mixed infections the average duration was forty-five days, for the pneumococcus cases thirty-five days, and for the streptococcus thirty-eight days.

2. *Remote Results.*—The chief interest lies in the possibility of tuberculosis. Of 13 cases of primary empyema in the writer's series, 4 have died—2 of "empyema" at intervals of six and eleven months after discharge, 1 of an unknown cause after one year and the last from intussusception. The remaining 9 patients are well at an average interval of four years after discharge. Of 26 patients with metapneumonic empyema, 7 have died—2

[1] Fatal cases are not included. The duration is short, for patients with sinus are discharged to a convalescent home.

of "empyema" after one and four years, 1 of "pneumonia," 1 of "tuberculosis," and the remaining patients from causes unconnected with this disease. Of the remaining 19 patients, 1 is known to have pulmonary tuberculosis, 2 others have had hæmoptysis, and a third has a persistent pleural sinus, seven years after discharge. The patients who are still alive have been followed for an average period of about five years.

## Special Forms of Pleuritis.

**Diaphragmatic Pleurisy.**—Pleuritis may be limited to the diaphragmatic region. It may be partial or general, fibrinous, serofibrinous, or purulent. Large collections of fluid are rare. Owing to its inaccessible site, physical signs are often lacking and the diagnosis may rest on symptoms alone. The pain may present features already described under fibrinous pleuritis, but is more likely to be referred to the lower thoracic or abdominal region. This may be due to implication of the lower intercostal nerves which supply the skin and muscles of the abdominal wall, as well as the parietal and diaphragmatic pleura. In the writer's series, abdominal pain was noted in 5 of 82 cases with primary fibrinous, in 5 of 374 cases with primary serofibrinous, and in 2 of 33 cases of primary purulent pleuritis. It may be associated with muscular spasm and tenderness, and the picture may simulate an acute abdominal affection for which laparotomy has been performed. Herrick[1] has recently emphasized its importance as a symptom of pleural and pulmonary disease. W. B. James suggests that aggravation of pain, following fixation of the thorax with straps, and its relief when the abdomen is similarly immobilized, may indicate the diaphragmatic site of pleurisy. There may be tenderness over the phrenic nerve in the neck or at the intersection of a vertical line parallel to the outer margin of the sternum and a horizontal line continuous with the termination of the tenth rib (De Mussy's Bouton Diaphragmatique). The breathing may be partially or wholly thoracic in type and the diaphragm phenomenon absent on one or both sides of the chest. Dyspnœa may be marked and attacks simulating angina may be observed (Andral). Obstinate singultus may occur. In a recent patient with diaphragmatic pleurisy in the writer's clinic, it was the principal trouble for which relief was sought. The phrenic and laryngeal branches of the vagus nerve are implicated and probably through irritation of the former in the diaphragm. The swallowing of food may cause pain.

**Encysted Empyema.**—Encapsulation of uncomplicated transudates does not occur. It is rare with serofibrinous fluid, but more common with pus. In occasional instances fluid may be serous in one and purulent in another pocket. Sacculation was discovered in only 1 of 1085 cases of serofibrinous effusion, but in 8 (3.2 per cent.) of 248 empyemas in the writer's series. It is, however, probably much more common than these figures show, for in 38 autopsies on patients with empyema it was noted in 12 (31.5 per cent.). Sacculation is more likely to occur in small or medium effusions and in those in which the fluid is at a standstill. Encapsulation may occur between (1) diaphragm and lung, (2) the lung and chest wall, and (3) the lobes of the lung.

[1] *Illinois Medical Journal*, 1903–4, N. S., v, 603.

1. **Encapsulation of Pus between Diaphragm and Lung** is more common than in other situations. In most instances the empyema is at first free, but is later walled off by adhesion of inflamed and apposed pleural surfaces in the posterior and inferior thoracic region. This was noted in five autopsies in the present series. Sacculation of fluid above the diaphragm without apposition to the thoracic wall may occur. The effusion may be bounded by lung and diaphragm, or by lung, diaphragm, and the mediastinum. Perforation of lung or diaphragm may be the first objective sign of the disease. The symptoms may suggest diaphragmatic pleurisy. The heart and the organs below the diaphragm may be dislocated, expansion of the affected side may be deficient, and on systematic examination of the chest an area of impaired resonance several inches above the base of the lung may be discovered. In this region diminished breathing, voice sounds, and tactile fremitus may be suggestive. Pleuritic friction may occur. If, as is often the case, more extensive pleuritis has preceded the sacculation, the physical signs may be difficult of interpretation.

2. **Sacculation between Lung and Chest Wall.**—This is not uncommon and likely to occur in cases in which a previous pleuritis has obliterated the diaphragmatic portion of the pleural sac. It is occasionally observed in empyema in which, following operation, the sinus has been allowed to close too quickly. Such encapsulation is more common over the base, but may be observed over other parts of the lung.

3. **Interlobar Empyema.**—Inflammation of the interlobar pleura occurs as part of a general pleuritis. An effusion of fluid may be limited externally by the thoracic wall, internally by the lobes of the lung between which it lies. In rare instances the effusion may not extend to the chest wall, and is bounded on all sides by the lung. Among others, Laennec, Martinez-Mesa, Pailhas, Potain, D. Gerhardt, Fränkel, and Musser have made contributions. The symptoms are not distinctive and the diagnosis is difficult. Examination may be negative and perforation of the lung may be the first indication. Rupture may take place as early as the fourteenth (Potain) or the nineteenth (D. Gerhardt) day. Dislocation of the heart may occur. In the affected region there may be dulness, diminished or absent breathing, voice sounds, and tactile fremitus. The localization of the process in the region of the interlobar septa and the absence of signs above and below this region are most likely to suggest the diagnosis. Examination by means of the *x*-rays may be of great assistance.

**Diagnosis.**—Laennec regarded œgophony as an important sign. Musser has recently emphasized the value of localized tenderness, which may be elicited only by firm and deep pressure in the interspaces. Sacculated, and especially interlobar empyema, is likely to be confused with pulmonary abscess. The gross character of the sputum may be suggestive. The sudden expectoration of a large amount of homogeneous pus, little mixed with mucus, may suggest empyema. The discovery in the expectoration of elastic tissue with an alveolar arrangement is diagnostic of pulmonary abscess, but does not exclude a complicating empyema. Tumors of the lung must also be considered. Exploratory puncture is usually recommended for the diagnosis but its danger has already been noted, and exploratory incision may be safer.

**Treatment.**—Perforation of the lung has been followed by spontaneous recovery. If perforation has already occurred when the patient comes under

observation, the decision between an expectant policy and operation must be made on the exigencies of the individual case. If the empyema can be reached, its evacuation is indicated.

**Actinomycosis and Nocardiosis of the Pleura.**—Two kinds of parasites must be recognized, *i. e.*, *Actinomyces bovis* and the *Nocardia*, the distinction between which has been pointed out by Wright.[1] Although the two parasites present well-marked biological differences, the clinical and pathological picture in infection is, in general, quite similar.

**Actinomycosis.**—In a large proportion of the cases this arises by extension from the lung. Pleural invasion may also occur from the œsophagus; by extension downward from the neck to the mediastinum and thence into the pleura; or from abdominal lesions which perforate the diaphragm. Metastasis is a possible mode of origin. The pleura overlying the involved tissue is the site of a fibrinous exudate. If adhesion of the visceral and parietal layers does not take place, a serofibrinous effusion or, more commonly, an empyema may result. The manifestations on the part of the pleura may mask the primary focus of the disease. Perforation of the chest wall is a characteristic feature. If, as often happens, pleural adhesion precedes the perforation, extension takes place through an obliterated pleural sac and the pleural changes are merely an incident in a more obvious disease of other organs. The thoracic wall may be involved without extensive changes in the pleura, or suppuration may similarly perforate the diaphragm by extension downward from the lung or upward from the abdomen, without invasion of the general pleural space. It is the site of single or multiple indurated and suppurating areas, connecting by means of sinuses with the pleura or the pleura and lung. Perforation may take place at any part of the thorax, but is more common in the lower thoracic region. Erosion of the ribs may occur. Amyloid degeneration may follow long-continued suppuration.

There is no distinctive clinical picture. Actinomycosis should be suspected in empyema, especially when associated with chronic pulmonary suppuration, interstitial pneumonia, abscess, gangrene, or empyema necessitatis. The diagnosis can be made only by finding granules with branching, Gram-staining filaments and radially disposed club-shaped, eosin-staining peripheral bodies. The prognosis is very unfavorable. A few arrested or apparently cured cases have been reported. The treatment is surgical, combined with the internal administration of large doses of iodide of potassium.

**Nocardiosis.**—This appears to be much less common. Infection of the pleura takes place by extension from the lung. The changes are similar to those in actinomycosis, and may closely resemble tuberculosis. The diagnosis is made by finding thread-like, branching organisms, which, in most cases, resist decolorization with weak acids and alcohol, but are less "acid-fast" than the tubercle bacillus, do not form granules or masses of closely packed interlacing filaments with the characteristic "clubs" at the periphery and are much more readily cultivated than either tubercle bacilli or actinomyces. In Birt and Leishman's case[2] an "acid-fast" streptothrix was recovered from the lung and the pleural pus. Lebram,[3] although he regards it as an infection with actinomyces, reports a case which appears to

[1] Vol. i, p. 327.

[2] *Journal of Hygiene*, 1902, ii, 120.

[3] *Ueber Miliar-Actinomykose der Pleura, Arbeiten auf dem Gebiete de Pathologischen Anatomie und Bacteriologie*, Baumgarten, 1904, Band iv, Heft 3.

belong in this group. There were multiple pulmonary abscesses and bilateral pleuritis. The left pleura contained gray, pearl-gray, or white nodules, resembling miliary tubercles, in which, as well as in the lungs, branching threads were found, but no tubercle bacilli. There were no typical granules. Cultures are not mentioned.

**Peripleuritis.**—Secondary inflammation of the peripleural tissue is associated with all pleural and many parapleural infections. A primary form has been described, in which, independent of neighboring disease, there is inflammation and suppuration of the tissue between the costal pleura and the chest wall. Wunderlich, Billroth, Bartels, Riegel, and others have described and recorded cases, but, as Martin suggests, with reliance on the clinical picture for the establishment of the group. Vogel[1] has recently reported cases in which at operation the disease appeared to be primary. Idiopathic peripleuritis is rare. It is usually localized and may be acute or chronic. Extension inward is uncommon, while perforation of the chest wall is frequent. There are the usual symptoms of suppuration. Movement of the affected side may be restricted. The tissue overlying the inflamed area is swollen. The involved region is dull, the breathing and fremitus diminished or absent. Fluctuation may be established. The diagnosis may be impossible before operation, and even then it may be difficult to distinguish between an encysted empyema and a peripleural abscess. A history of preceding pleural disease may suggest the former. The absence of signs of disease at the base of the chest, slight or failing dislocation of the heart and the lack of shifting dulness may distinguish between peripleural abscess and ordinary empyema. The prognosis has been regarded as unfavorable. Early diagnosis followed by prompt and appropriate surgical treatment may be expected to give favorable results in simple (non-tuberculous) and uncomplicated cases.

**Chronic Pleuritis.**—1. **Dry Pleurisy.**—This occurs as a sequel to fibrinous, serofibrinous, or purulent pleuritis. Even in the mildest cases of fibrinous pleuritis the pleura rarely escapes some damage. The pleura overlying a pulmonary process may be merely thickened. Adhesions between the pulmonary and parietal layers are common. On postmortem examination these may consist of delicate, thread-like connections, or as circumscribed or general synechiæ on one or both sides of the chest. The lung may be extensively torn in removal unless a dissection is made. The pleura may reach a centimeter or more in thickness and enclose single or multiple pockets of serous or purulent fluid. Deposition of lime-salts may have taken place. The neighboring lung is often contracted and fibrous in character. Bronchiectatic or abscess cavities are frequently found. The interstitial pulmonary changes may be due to extension from the pleura, but it is difficult in individual cases to exclude their independent origin. The pleural changes may be simple or tuberculous. In the latter instance, small tubercles, fibrocaseous or calcified areas may be found in the indurated tissue. The site of the process is usually at the bases, when it follows pleurisy with effusion. In tuberculous cases it is frequently at the apices, and extensive pleural thickening may complicate slight pulmonary infections.

There may be no symptoms. Pain of varying and usually slight intensity may be present. Pleuritic friction may exist without subjective symptoms.

[1] *Deut. Zeit. f. Chir.*, 1902–03, lxvi.

Adhesions usually prevent the rubbing of the two pleuræ together, however, and the signs are such as have been mentioned under Sequelæ in the preceding sections. Chronic apical pleuritis may give rise to depression of the supra- and infra-clavicular fossæ, to contraction of the apex, dulness, diminished breathing, voice sounds, and tactile fremitus, but co-existent pulmonary lesions may make the signs of thick pleura atypical. The finding of chronic dry pleurisy at the bases need occasion no anxiety when it is known to have followed a pulmonary disease which has run a favorable course. An apical process is tuberculous in a large proportion of the cases. If pulmonary tuberculosis is suspected, suitable treatment should be instituted. With retraction of the side and fixation of the lung, pulmonary gymnastics will favor expansion and improve the breathing capacity.

2. **Pleurisy with Effusion.**—In rare instances serofibrinous or purulent fluid continues to re-accumulate after repeated thoracentesis or operation.

(*a*) *Serofibrinous Form.*—Persistent re-accumulation may be due to failure of the retracted and adherent lung to expand and a neglect of early tapping may be responsible. In some cases this appears not to be the cause, and West[1] noted in two instances, with a duration of eighteen months, that the lung was still capable of re-expansion. In the absence of malignant disease and obvious pulmonary tuberculosis, a resort to operation may be considered after other measures have been tried. It should be advised with caution, however, for it necessarily induces empyema, which may also fail to heal, if the lung is adherent. West has had two successful cases. He regards pulmonary adhesions as a contra-indication.

(*b*) *Empyema.*—In this, as in the serofibrinous form, after the pus has remained long in the chest, the lung may be partially or wholly incapable of re-expansion from the presence of abundant connective-tissue formation in and about it. After operation and the evacuation of pus, a space is left, and in the young, with less resistant thoracic walls, marked deformity, retraction of the side, and lateral deviation of the spine may result. At times, from the stiffness of its walls, the abscess cavity refuses to close, and cure can be effected only by more extensive operative procedures. In many cases the first operation has been too long delayed. Multiple costatectomy (the so-called Estlander's operation) may be considered in persistent partial, but is not likely to succeed in large or total empyema, in the presence of greatly thickened parietal pleura or in old patients with unyielding thoracic walls. In such cases, Schede's "Thoraxresection" may be successful.

## HYDROTHORAX.

Transudation of serous fluid into the pleural sacs occurs in the course of many diseases, but when in sufficient amount to be detected during life, is usually secondary to renal or cardiac disease. Renal disease alone gives rise to only small amounts of pleural fluid, but is often combined with cardiac insufficiency. Local stasis is probably a contributing factor in connection with new-growths of the pleura, lung, or diaphragm. Occlusion of the azygos veins from pressure or thrombosis is a possible cause.

Cardiac insufficiency may give rise to fluid in one or both pleural sacs,

[1] *Lancet*, March 25, 1905.

with or without general dropsy. Cardiac hydrothorax is commonly unilateral and right-sided, and when both pleuræ are affected the amount of fluid is usually greater on the right. Of 17 cases in Stengel's[1] series the effusion was bilateral, but greater on the right in 9, unilateral and right-sided in 5, and confined to the left side in only 3, in 2 of which the right pleura was obliterated. Of 30 cases of cardiac hydrothorax in the writer's series, the effusion was bilateral in 8 cases, in 6 of which the amount of fluid was greater on the right and equal on the two sides in the remaining 2. It was unilateral and right-sided in 16, and confined to the left side in only 6. The predominance of right-sided accumulations is too constant to be accidental or to be explained by previous pleuritis and obliteration of the left pleura, which can account for only a small proportion of the cases. It is probably due to pressure of the dilated right auricle, right ventricle, and vena cava, and the displaced root of the lung on the azygos vein, as suggested by Stengel. Hydrothorax from renal disease alone is usually bilateral. If, as often happens, the heart is insufficient, the accumulation may be unilateral and right-sided or double with an excess on the right. Of 15 cases in the writer's series, the effusion was bilateral in 7, in 2 of which the amount was greater on the right, in 3 on the left, and equal on the two sides in the remaining 2. It was unilateral and right-sided in 6 cases, of which 5 were complicated by cardiac lesions. The effusion was confined to the left side in 2 cases.

If the decubitus is prevailingly lateral, a larger amount of fluid may collect in the dependent pleura. The pleura may be smooth or slightly clouded and swollen. Old adhesions may limit the accumulation to single or multiple pockets. The fluid is usually clear and yellowish, but may be reddish from admixture of blood. It clots slowly or not at all, and fibrin is absent in uncomplicated cases. The specific gravity in venous transudates is usually from 1010 to 1015, with 1 to 3 per cent. of albumin, while hydræmic fluids are below 1010, with traces to 1 per cent. of albumin. The sediment usually shows an excess of endothelial cells. In rare instances lymphocytes may predominate. A complicating pleuritis is not uncommon, and polynuclear cells may then outnumber the other elements.

**Symptoms.**—The symptoms are those of the underlying disease. Pain is absent. If there is fever, it cannot be ascribed to hydrothorax. Cough and expectoration may be due to œdema of the lungs. There may be gradually increasing dyspnœa, which may amount to orthopnœa. The signs are the same as with pleural fluid of other character. Pleuritic friction is absent. Shifting dulness is more readily obtained. Rosenbach and Pohl[2] find that even small amounts of iodine or its salts given by mouth can be demonstrated in transudates, but not in exudates. The test is performed by adding fuming nitric acid to fluid obtained by puncture and agitation with chloroform, which is turned red if the test is positive.

**Treatment.**—The treatment is that of the underlying disease. Removal of the fluid by thoracentesis is indicated, if necessary, for the relief of an embarrassed circulation or breathing.

[1] *University of Pennsylvania Medical Bulletin*, June, 1901.
[2] *Berl. klin. Woch.*, 1890, Nr. 36.

## HEMORRHAGIC PLEURAL FLUIDS.

Microscopic blood is always present in pleural fluids. Small amounts of blood may arise from puncture of the lung in thoracentesis. Larger quantities of fresh blood color the fluid reddish or even blood red. Dieulafoy estimates that 5000 to 6000 red cells per cc. are necessary to give the fluid a definitely red color. Only cases with frankly hemorrhagic fluid are considered here. In old extravasations the fluid may assume a reddish-brown, yellowish, or greenish color. Clinically, it is convenient to divide bloody fluids into hæmoserothorax (hemorrhagic pleurisy), hæmohydrothorax, and hæmothorax.

**Hæmoserothorax (Hemorrhagic Pleurisy).—Primary.**—(*a*) *Tuberculous.*—An apparently primary disease of the pleura with the production of serohemorrhagic fluid is tuberculous in a great majority of cases. (*b*) *Malignant.* In a relatively small proportion of cases it is due to carcinoma, rarely sarcoma. A discussion of these causes will be found elsewhere. In both groups it is not infrequently observed that the effusion becomes more bloody with successive tappings. (*c*) *Simple Hemorrhagic Pleurisy.* There is no sound pathological evidence in support of this group, as a primary affection, although hemorrhagic fluids of secondary and infectious origin are not uncommon. The clinical cases with an apparently primary hæmoserothorax, which appears to be of simple origin, practically always run a clinical course consistent with tubercle or malignant disease, or show one or the other of these conditions at autopsy. There are a few striking exceptions as regards a more favorable clinical course. Osler[1] refers to a large, able-bodied man, with hemorrhagic exudation, who was healthy and strong eight years afterward. Cheesman and Ely[2] report a most remarkable instance in a woman aged forty-seven years, with bloody fluid first in the right, then with similar fluid in the left chest, and finally, following the disappearance of this fluid, with bloody serum in the abdomen. The pleural accumulations continued for about eighteen months, and no chest difficulty arose in the following seven years, but in this interval the abdomen was repeatedly tapped. The abdominal fluid ceased to re-accumulate after about five years, and at the date of the report twenty months had elapsed without recurrence. There was a large fibroid of the uterus. In all, two hundred and seventy-nine pints of fluid were removed.[3]

**Secondary.**—This is a much more common form. Cases due to tuberculosis, although they may seem clinically to be primary, are usually secondary. So, also, in hemorrhagic pleurisy due to malignant disease, the primary form is rare, that from metastasis relatively common. Cases not included in these two groups may be classed, as in the primary form, as simple hemorrhagic pleurisy. Hemorrhagic serofibrinous effusions of this sort are perhaps most common in pneumonia, and are usually due to the pneumococcus. Of 57 cases of croupous pneumonia, showing pleural effusion at autopsy in the Massachusetts General Hospital, the exudate was bloody in 6. In none of these was there evidence of tuberculosis of the pleura. An inflammation

[1] *Practice of Medicine*, 1905, p. 651.
[2] *American Journal of the Medical Sciences*, August, 1899.
[3] Cheesman, now, 1907 (seventeen years from the onset), informs the writer that the patient is entirely well.

of the pleura in the course of malignant fevers (variola, typhoid) in purpura hemorrhagica or complicating such asthenic conditions as accompany malignant disease, nephritis, cirrhosis of the liver or chronic heart disease, may be of the hemorrhagic variety, whatever the cause of the process in the pleura. Some prove to be tuberculosis; others are simple and due to the pneumococcus or pyogenic organisms, the blood in the exudate being due to passive congestion or the intensity of the local process.

An interesting feature of the hemorrhagic pleural fluids is the high percentage of eosinophiles which they may contain and the presence, also, of a large number of eosinophiles in the circulating blood. In Klein's case[1] (autopsy but no microscopic examination of the tissue) the pleural fluid showed 76.4 per cent. eosinophiles (small lymphocytes, 23.6 per cent.), the systemic blood 40 per cent. of eosinophiles. In Harmsen's case[2] the pleural fluid showed 8.64 per cent. eosinophiles (small lymphocytes, 87.65 per cent.). In a case of apparently primary disease of the pleura in the writer's series, the bloody pleural fluid showed no excess of eosinophiles, but contained enormous numbers of cholesterin crystals, while the systemic blood showed 6400 white cells, of which 20 per cent. were eosinophiles.

**Hæmohydrothorax.**—Transudates may have a hemorrhagic character in cardiac or renal disease. Thrombosis of the thoracic veins or their occlusion by pressure of tumors is a possible cause. In Zahn's case[3] there was thrombosis of azygos and intercostal veins and hemorrhage. Zahn was unable to cause similar changes by experimental obliteration of the azygos veins.

**Hæmothorax.**—This may be due to the rupture of intrathoracic vessels following the development of aneurism, their erosion by disease or injury by trauma. In the rupture of the aorta or its ulceration the left pleura is more often the site of the hemorrhage. The pulmonary veins and the vena cava may rarely be the source. The rupture of pulmonary vessels from destructive pulmonary processes may rarely lead to hemorrhage into the pleural sac. The intercostal arteries may, likewise, be eroded in disease of the pleura. There is a specimen (No. 2159) in the Warren Museum from a patient with empyema, in whom erosion of an intercostal artery led to fatal hæmothorax. The lungs showed tuberculosis.

**Traumatic Hæmothorax.—Etiology.**—This may arise from contusions of the chest, more often from fracture of the ribs, and most commonly from incised or penetrating wounds. The bleeding may come from injured vessels in the thoracic wall, more rarely small branches of these parietal vessels. Owing to the protected position of the intercostal arteries, their injury is relatively uncommon. In a large proportion of cases the hemorrhage is from a wound of the lung, superficial injuries of which may lead to varying and usually insignificant hæmothorax, deeper wounds to abundant hæmothorax, if an important vessel is involved. The injury of vessels accompanying bronchi of the second or third order may be followed by hemorrhage compatible with survival.[4] Wounds of vessels about the hilus of the lung and the larger mediastinal vessels are followed by rapidly fatal hemorrhage.

**Special Pathology.**—(*a*) *Onset of Hemorrhage.*—Following the injury of the larger bloodvessels, fatal hemorrhage into the pleura may occur within

[1] *Cent. f. innere Med.*, January 28, 1899. [2] Quoted from Klein.
[3] Virchow's *Archiv*, 1885, p. 345.
[4] Nélaton, "Des épanchements de sang dans les plèvres, etc.," *Thèse de Paris*, 1880.

a few minutes. An effusion of blood from the parietal vessels and the lung usually begins at once and is slowly continuous. In the more favorable cases the bleeding usually stops after twenty-four to forty-eight hours. Delayed hemorrhage is rare. In Nélaton's series of 94 cases a secondary and fatal hemorrhage followed a gunshot wound of the chest, in 4 cases, on the second, the tenth, the twelfth, and the thirty-sixth day respectively. In Vialle's and Braun's case, following a knife cut in the second left intercostal space, hæmothorax due to the rupture of a traumatic aneurism of the internal mammary occurred on the nineteenth day.

(*b*) *Time of Coagulation.*—In experimental work the introduction of artificial conditions limits the value of the observations. Nélaton caused hæmothorax in animals by injuring the lung with a knife, and found that the extravasated blood coagulated within twenty-four hours, as shown by autopsy. His experiments were not performed under aseptic precautions. Penzolt[1] found, in fourteen experiments, that the blood at first remains fluid, that large effusions coagulate after two hours, and that small amounts of blood coagulate at the latest after twenty-four hours. Pagenstecher[2] found, in nine experiments, that blood injected into the pleural cavity is still fluid after about two hours, while clots and uncoagulated fluid are present after about six hours. The reports of surgical interference and the autopsy table, although not numerous, suggest that coagulation of the effused blood invariably occurs in man and probably within an equal period. It is frequently noted that hemorrhagic pleural fluid does not coagulate on removal, and this is probably due to its previous coagulation within the chest.

(*c*) *Absorption.*—In favorable and uncomplicated cases the fluid is wholly absorbed. The blood clot becomes adherent to the pleural surfaces, softening and organization take place, and after small extravasations, nothing but a few adhesions may remain. With large hemorrhages and much clot, more extensive adhesions and thickening of the pleura persist. The affected side may show diminished expansion.

(*d*) *Occurrence of Pleuritis.*—The extravasation of blood is not in itself a cause of pleuritis, and when infection occurs in hæmothorax, it is due to bacteria which have invaded the pleural sac from without, through the thoracic wound or the lung. The incidence of suppuration in traumatic hæmothorax is uncertain, from the lack of any series of unselected cases of sufficient number dealing with this point. Its occurrence can, therefore, be formulated only in a general way. It appears to be less frequent in small effusions, and is less likely to occur following injuries of the parietal vessels or the superficial parts of the lung, without an external wound. Large effusions of blood, those arising from incised or penetrating wounds, and hemorrhage from the deeper parts of the lung, often become purulent.

(*e*) *Examination of the Pleural Fluid Obtained by Puncture.*—Observations are rare on this point. The number of red cells progressively diminishes in the effused blood. This is partly due to the dissolution of red cells in the fluid, to phagocytosis by endothelial cells, and to sedimentation, counts in fluid taken from different levels showing fewer reds and a larger number of white cells above, while the opposite is true below. In judging the presence

[1] *Deut. Archiv. f. klin. Med.*, 1876, p. 542.
[2] *Beiträge zur klinischen Chirurgie*, Tübingen, 1895, 13, p. 264.

of an infection from an enumeration and differential count of the white cells, due allowance must be made for the number of polynuclear cells in the effused blood. In De Gery and Froin's case of traumatic hæmothorax, a differential count of the white cells in the effused blood showed: large mononuclear cells, 90.42 per cent.; lymphocytes, 2.12 per cent.; polynuclears, 3.72 per cent.; eosinophiles, 3.72 per cent. Three days later the eosinophiles numbered 28.76 per cent. In Harmsen's case there was a marked systemic leukocytosis with eosinophiles in both systemic and pleural blood.

(*f*) *Relation with Tuberculosis.*—Hemorrhagic pleural effusion following trauma may rarely be tuberculous. Lustig[1] relates the case of a laborer of forty-three, without tuberculous antecedents, in whom a left-sided hemorrhagic effusion followed a fall, striking the left chest against a wheel. Death occurred one month later. Autopsy showed tuberculosis of the left pleura.

**Symptoms.**—In some cases there are no symptoms, most likely in small and slowly accumulating effusions. Shock is a variable feature. Pressure symptoms usually occur within twenty-four hours and are rarely delayed for forty-eight hours. In one of Nélaton's cases the hemorrhage was delayed for thirty-six days. With the rapid accumulation of a large amount of blood, death may ensue within a few minutes. In most cases there is slowly increasing dyspnœa, which is the most constant symptom, due to collapse of the lung and consequent dislocation of the mediastinum. Pain may be present, and is usually referred to the affected side. Cough is an inconstant symptom. If the lung is wounded there is likely to be hæmoptysis. The blood in the sputum may consist of blood streaks, or there may be frank hæmoptysis. In addition, with the more rapid accumulation, there are symptoms due to loss of blood, pallor, progressive elevation of the pulse, with alteration in its quality, coldness of the extremities and body, and sweating. Syncope or delirium may occur. The temperature may be subnormal at first, and in favorable cases may not exceed normal limits. In a considerable proportion of cases the temperature rises, after the first or second day, a degree, a degree and a half, or even two degrees Fahrenheit, and remains thus elevated for several days. Although such an elevation of temperature naturally occasions much anxiety, such cases not infrequently progress favorably. The rise in temperature may be due to absorption.

The physical signs of hæmothorax need not be especially referred to here, as they differ in no respect from the signs with pleural fluids of other character.

**Complications and Sequelæ.**—Infection of the effused blood is most to be feared. Although there are no trustworthy statistics concerning the frequency with which empyema develops, yet it appears from Nélaton's 94 collected cases that the effusion became purulent with more or less certainty in 21. Hæmopneumothorax is common, and may become pyopneumohæmothorax. Pneumonia, pulmonary abscess, or gangrene may arise from the injury or follow as a result of neglected empyema. The rupture of traumatic aneurism of the internal mammary artery was the apparent cause of hæmothorax, which developed nineteen days after the injury in Vialle and Braun's case. Recovery followed ligation of this artery. An unruptured aneurism of the same artery was found after death in

[1] Quoted from Trouvé, *Thèse de Paris*, 1902.

De Montegre's case. In both there was localized pulsating tumor, and in the former a systolic murmur.

**Diagnosis.**—A careful physical examination should always be made when patients with chest injuries first come under observation. A neglect of this precaution may lead to unnecessary delay in the diagnosis of an empyema. A pleural effusion developing within a few hours of a thoracic injury means hæmothorax with practical certainty; a delayed effusion is usually inflammatory, rarely hemorrhagic. The early detection of infection is most important. Evidence of its occurrence is usually afforded by elevation of temperature, which commonly takes place from the third to the fifth day, and is accompanied by other symptoms of sepsis, such as are ordinarily seen in empyema. Symptoms of sepsis may develop, however, only after days or weeks have elapsed. The presence of an infection may be suspected when, even without fever, there is a delay in the absorption of the fluid, which in most cases progressively diminishes in amount, and moderate effusions may be fully absorbed within a month. Any increase of a fluid which has previously reached a standstill should likewise be regarded as due to inflammation and not recurrent hemorrhage, which is relatively uncommon. An enumeration of the white cells in the systemic blood at intervals may be of value in the early recognition of suppuration. An initial leukocytosis may be due to hemorrhage alone.

Exploratory puncture and the withdrawal of sufficient fluid for diagnosis should be done if empyema is suspected. If the puncture is made at a distance from the original injury there is less danger of dislodging an occluding thrombus. The trocar should be inserted toward the upper rather than the lower level of the fluid, to avoid a dry tap from penetration of the clot. If properly performed, and under rigidly aseptic precautions, the procedure is practically devoid of danger. The presence of an infection may be sufficiently obvious from inspection of the fluid. In developing or mild infections the microscopic examination of the sediment may show an excess of polynuclear cells and may also show that degenerative processes are at work from their necrotic appearance. Cultures should be taken.

**Prognosis.**—Traumatic hæmothorax is always serious. The site, extent, and character of the original injury, the rapidity with which the hemorrhage takes place and the amount of effused blood are important factors in prognosis. In some cases the effusion of blood may be small, and pneumothorax may be the significant feature. To these dangers that of infection is added. Of Nélaton's 94 cases of traumatic hæmothorax, gathered from the older literature, 49 died from immediate or remote causes. The seriousness of chest injuries, in general, can be gathered from the cases collected from the literature by Garrè.[1] In 37 cases of pulmonary rupture the mortality was 63 per cent., in 100 cases of punctured wounds, 38 per cent.; in 535 bullet wounds, 30 per cent. Hemorrhage, pneumothorax, or infection are the principal causes of death.

**Treatment.**—The cases come within the province of the surgeon and their treatment can be considered here only in a general way. Aside from the surgical care of external wounds an expectant policy has for the most part been followed hitherto in cases without alarming symptoms. The patient should be absolutely at rest. Immobilization of the affected side by strips of adhesive plaster may favor cessation of the hemorrhage. The

[1] *Archiv f. klin. Chir.*, 1905, lxxvii, p. 209.

administration of lactate of calcium, 15 gr. (1 gram), four times a day, may be of value. The hæmothorax if uninfected will be absorbed. If suppuration occurs, the empyema should be opened and drained. The large proportion of deaths from hemorrhage, from suffocation by hæmothorax or pneumothorax, and the frequency with which the pleura becomes infected, leaves much to be desired from surgery in the care of such cases.

Although the cleaning and disinfection of external wounds may be secured, and doubtless eliminates a small measure of infection, there still remains the considerable danger of infected material already carried into the thorax or arising in consequence of a communication between the lung and the pleura. In cases with alarming symptoms and for the present as a life-saving measure, a more active surgical intervention may properly be considered. A source of the hemorrhage in a parietal vessel may at times be determined from the site of the injury. The lung itself is, however, more often the source, and then surgery is less likely to be successful. The lung is likely to be partly or wholly collapsed and the bleeding wound difficult to find or to reach. Suture of the lung has as yet been too infrequently performed to furnish trustworthy statistics. Garrè, in 1905, collected 9 cases with 6 recoveries.

Thoracentesis and the slow withdrawal of blood has been advised, for the most part by French surgeons, for alarming pressure symptoms following hæmothorax. Bourgeois[1] was able to collect 9 cases in which thoracentesis was performed on the first to the fourth day, with recovery. No unfavorable cases are mentioned. The measure is regarded not only as palliative, but also as curative, on the theory that the collapsed lung is congested and thus bleeds more readily than otherwise. In cases obviously suffering from pressure and without marked symptoms of hemorrhage, the procedure may be tried.

## CHYLOTHORAX.

**Chylous and Chyliform Pleural Fluids.**—Much confusion still exists in the classification of milky fluids which may accumulate in the serous sacs. Quincke,[2] in 1875, grouped the cases into those with chylous fluid (hydrops chylosus) in which the appearance was due to the presence of true chyle, and a second class with fluid of a chylous appearance (hydrops chyliformis seu adiposus), the milky character being due to cells undergoing fatty degeneration. He believed that it was easily possible, by microscopic examination, to differentiate the two forms. Unfortunately, however, further experience has shown that the distinction is often difficult and at times impossible. The two types of fluid may be present in different cases, both of which are due to a similar cause, and a single sample of fluid may likewise present features common to both forms. The differentiation from the presence of sugar, which, in more than questionable traces, Senator[3] regarded as an indication of the chylous nature of the fluid, cannot be relied upon, since Rotmann[4] showed that serous fluids (without chyle) may also contain from 0.055 to 0.112 per cent. of sugar. Rotmann believes that sugar is

[1] "Traitement par la ponction de l'hemothorax traumatique," *Thèse*, Lyon, 1905.
[2] *Deut. Arch. f. klin. Med.*, Band xvi, pp. 121 to 139.
[3] *Charité-Annalen*, xx, p. 263.
[4] *Zeit. f. klin. Med.*, 1896, xxxi, p. 416.

a differential sign of importance only when present in an amount exceeding 0.2 per cent.

Such fluids are white and milky in appearance, but may be reddish from the presence of blood or show varying shades of yellowish or greenish color. In the last instance they may readily be mistaken for purulent fluid. They are usually odorless, but may be slightly sweetish. Thin layers are opalescent. On standing a creamy layer of fat collects at the surface. They are resistant against putrefaction. Their milky appearance is maintained after filtration or centrifugalization, but they can be cleared by shaking with ether. From 0.06 to 3.71 per cent. of fat have been extracted. The amount of albumin is variable; from 3.36 to 7.37 per cent. has been reported, with traces of casein in one instance. Solids are present from 5 to 10 per cent., inorganic substance (salts and extractives) about 1 per cent. Fibrin is variable—present in some, absent in other cases. Cholesterin, lecithin, calcium, magnesium, potassium, sodium, chlorine, and carbonic, sulphuric, and phosphoric acids have been found. Microscopic examination discloses a large number of minute fat droplets about the size of micrococci, but readily differentiated from microörganisms. In the chylous fluids the fat granules are very numerous, with only few formed elements, while the chyliform fluids contain less numerous fat granules, of larger size, and more numerous cells in different stages of fatty degeneration.

**Pseudo-chylous Fluids.**—Pleural fluid may have a milky appearance without the presence of fat. Quincke showed that albumin in fine subdivision may cause a milky appearance. Lion,[1] in 1893, showed that fat was absent in a milky abdominal fluid which he studied. An albuminous body was found, the nature of which was uncertain. Such substances have been regarded as lecithin, globulin, casein, or a compound of globulin and lecithin. These pseudo-chylous fluids are distinguished from the chylous and chyliform fluids by the separation of the latter into two layers on standing, while the former remain homogeneous. The microscopic examination of chylous or chyliform fluids shows the presence of fat, which may be stained black with osmic acid or removed on shaking with ether. In gross appearance chylous and chyliform fluids may resemble purulent fluids, from which they can be differentiated by more careful examination.

**Occurrence.**—The presence of chylous or chyliform pleural fluids is of infrequent occurrence. It is probable that they are more common, however, than the number of reported cases indicates, since chylous may be readily confused with purulent fluid, unless carefully examined. Bargebuhr[2] was able to collect 41 cases, reported from 1633 to 1894, an incidence of 1 case reported about every six years. Rotmann in 1896 brought the number up to 49.

**Etiology.**—Of 40 cases in Rotmann's series, in which the cause could be determined, 27 were classed as chylous, 13 as chyliform. Of the chylous cases, 8 were due to trauma; 5 to cancer of the pleura; 4 to occlusion of the left subclavian vein. Two cases were ascribed to each of the following causes: compression of the duct by tumors, disease of the lymph vessels (sclerosis, lymphangiectasis), and malignant lymphoma, and 1 case to each condition as follows: occlusion of the thoracic duct, excessive exertion and parasites (filaria?). The presence of chyliform fluid, with admixture of fatty de-

[1] *Archiv de méd. experiment.*, 1893, No. 6, p. 826.
[2] *Deut. Archiv f. klin Med.*, 1895, 54.

generated cells, was due to cancer of the pleura, lymph vessels, etc., in 5; tuberculous pleuritis in 3; exudative (non-tuberculous) pleuritis in 3; and pulmonary abscess (?) in 1. One case was regarded as the result of an abnormal amount of fat in the blood (lipæmia?).

**Diagnosis.**—The chylous or chyliform character of a pleural fluid can be determined with certainty only by an examination of the fluid. Its presence may be suspected, however, following trauma, with malignant disease of the pleura, glands, or lymphatics, and with thrombosis of the left subclavian vein. The association of pleural fluid with the known presence of chylous ascites may suggest a chylous character to the former. Uncomplicated cases of chylous or chyliform pleural fluid are usually afebrile. Such an accumulation may occur at any age and in either or both pleural sacs.

**Prognosis.**—*Chylous Fluids.*—The transudation of chyle into the pleura adds to the danger of the underlying disease, from the additional tax on the patient from the loss of food which would otherwise be utilized in the system. Thus the course of an affection steadily progressing toward a fatal termination may be hastened. The rapidity and extent of the accumulation are important for the estimation of its effect on the patient. Small accumulations, the removal of which is unnecessary, probably add little to the danger of the original disease. The prognosis becomes more unfavorable when the frequent recurrence of alarming pressure symptoms necessitates the repeated withdrawal of large amounts of chylous fluid. The underlying cause is usually of so grave a nature that in general the prognosis must be considered unfavorable. Of 22 cases (11 classed as chylous, 11 probably chylous) in Rotmann's series only 4 recovered. Of these, 2 were due to trauma, 1 to probable disease of the lymph vessels, and the last to an uncertain cause.

*Chyliform Fluids.*—The prognosis in cases with chyliform pleural fluid is more nearly that of the underlying cause, such cases being due to the fatty degeneration of existing cells.

In cases with chylothorax in which recovery has followed it is probable that the chylous transudation has come from branches of the main thoracic duct or that the occlusion of the latter is compensated by an abundant collateral circulation. Slight lesions of the thoracic duct may heal and the duct remain patent.

*Traumatic Chylothorax.*—Such cases present features of special interest from their rarity and more favorable prognosis. Only about 11 cases are recorded in the literature. The chylothorax was double in 1 case (Henssen), left-sided with right hæmothorax in 1 (Handmann's first case), right-sided with left pneumothorax in 1 (v. Thaden), and confined to the right side in the remaining 8 cases (Quincke, Kirschner, Krabbel, Helferich, Handmann, Hahn, Dietze, and Lindstrom). The traumatic cases may be fatal from the original injury plus the mechanical effect of the pleural fluid, or in time from a loss of lymph.

In 1 of the reported cases (Dietze) an injury to the thoracic duct followed a self-inflicted bullet wound. In the remaining cases the chylothorax was due to severe mechanical injury to the thorax, with certain or probable fracture of the ribs. In 2 of the 5 fatal cases the thoracic duct was found to have been injured by fragments of the tenth and eleventh dorsal vertebræ respectively. The mechanism of the injury to the duct in the other cases is uncertain. It may have been lacerated or ruptured by bony fragments of the ribs or vertebræ, or compressed between the mediastinal structures and

the vertebral bodies with sufficient force to injure it, without injury to the more resistant neighboring structures (aorta, azygos vein, œsophagus). In these cases the implication of the parietal pleura in the injured structures is indicated by the presence of chylous fluid in the pleural sac. Rupture of the thoracic duct may, however, lead to an accumulation of chyle outside the pleural sac provided the parietal pleura is uninjured. Under these circumstances the mediastinum may be infiltrated or the parietal pleura dissected up from the thoracic wall, as in Eyer's case.

**Treatment.**—This presents a somewhat different problem from other pleural fluid, since the diminution of pleural pressure favors re-accumulation and changes in pressure interfere with the healing of lesions of the lymphatic vessels. The repeated loss of large amounts of such fluid is a severe drain. It is best, therefore, in the presence of small amounts of such fluid to keep the patient under observation after sufficient material has been withdrawn for diagnostic purposes. Strapping the affected side may prevent an increase of the fluid by diminishing the respiratory changes in intrapleural tension. In the traumatic cases an expectant policy was followed by spontaneous absorption of the fluid in two instances (cases of Henssen and Handmann). When an excessive amount of fluid has accumulated it must be evacuated with the trocar. This was done in 6 cases, with 3 deaths (cases of Quincke, v. Thaden, and Hahn) and 3 recoveries (cases of Kirschner, Handmann's second case, and Dietze). In Hahn's fatal case, twenty-nine liters of fluid were removed within twenty-six days. Dietze's patient recovered after the withdrawal of twenty-seven liters in thirty-one days. If possible, operation should be delayed until the level of the fluid has ceased to rise. It is better to remove small amounts frequently than a large amount at one time. In 1 case (Krabbel) the fluid, six liters in amount, was first discovered at autopsy. Because of the inaccessible site of the thoracic duct an attempt at its ligation is hardly likely to prove successful. An increase of intrapleural pressure to that of the atmosphere, following resection of a rib, may effect a cure. Thoracotomy was followed by recovery in one case (Helferich) and death in another (Lindstrom).

## TUMORS OF THE PLEURA.

A. **Benign Tumors.**—These are rare and without a distinctive clinical picture. They usually run their course undetected during life, and are first discovered at autopsy. In general they consist of tumors arising in neighboring organs which invade the pleura by encroachment, usually remaining extrapleural, at times projecting into the pleural space, but enveloped by its visceral or parietal layer.

Aberrant lung tissue may project into the pleural space. In a case described by Muus,[1] a smooth tumor the size of a walnut was found in the left pleural cavity, attached to the diaphragm and covered by diaphragmatic pleura. The tumor showed on section an alveolar arrangement. The alveolar septa contained vessels and fine muscle fibrillæ. Connective tissue, cartilage, elastic fibers, and ciliated cylindrical epithelium were also present. Small single or multiple cysts of the pleura are described by

[1] *Virchow's Archiv*, clxxvi, p. 180.

Stilling[1] and Zahn.[2] Their walls contained cartilage and acinous glands, lined with ciliated epithelium, suggesting their origin from the bronchi. Emphysema may give rise to cyst-like structures projecting into the pleural cavity, the so-called bullous marginal emphysema. A specimen in the Warren Museum (No. 2142) shows such a bleb, the size of a horse-chestnut, its walls composed of thickened pulmonary pleura, lined with delicate trabeculæ and connecting with the bronchi. They may reach a much larger size. Their rupture may give rise to pneumothorax. Pulmonary adenoma, angioma, or osteoma may invade the pleural sac. Fibroma may arise in the lung and similarly invade the pleura.

**Lipoma.**—Fatty tumors may rarely arise from the subpleural fatty tissue and project into the pleural sac. They are usually too small to give rise to symptoms or physical signs, and are discovered at postmortem examination, growing from the costal, diaphragmatic, or mediastinal fatty tissue as rounded or flattened, sessile or pedunculated masses. Fitz[3] has reviewed the literature and reported a case. In rare instances, lipoma of the thoracic wall may communicate with the subpleural space and project into the pleural sac, as in the cases of Czerny,[4] Plettner,[5] Gussenbauer,[6] and Krönlein.[7] Such possible communication through the thoracic wall with the thoracic cavity should be borne in mind in operations for the removal of subcutaneous lipomas, as infection of the wound may readily lead to infection of the pleura. In Krönlein's case, a female infant of one year, a lipoma occupied a large part of the front of the right chest; at operation it was found to be continuous by a pedicle the size of the thumb, passing through the third interspace 1 cm. from the right sternal margin, with a similar growth, as large as a child's head, almost entirely filling the anterolateral portion of the left thoracic cavity. In Fitz's case a lipoma about the size of a newborn child's head was found at autopsy in the inferior and lateral portion of the left pleural cavity and apparently continuous with the fat tissue of the superior mediastinum. It was apparently covered by the pleura, and was adherent to the diaphragm, pericardium, and parietal pleura. The mass obscured an acute purulent pericarditis arising in the course of lobar pneumonia.

B. **Primary Malignant Disease.**—1. **Carcinoma.**—**Synonyms.**—Endothelioma; endothelioma lymphangiomatosum; pleuritis carcinosa; lymphangitis carcinomatodes; lymphangitis prolifera; sarcocarcinoma. Although the term endothelioma has been most commonly applied, carcinoma seems more appropriate. The general character and histological appearance of the tumor do not, in general, sufficiently differ from carcinoma in other regions, and its origin in the surface epithelium or lymph-vessel endothelium is too uncertain to warrant a more distinctive term.

**Occurrence.**—This is a rare affection, of which some 40 to 50 cases are sufficiently well recorded to permit of acceptance.[8] The writer has had opportunity of studying sections from 3 cases.[9] It is probable that the

[1] *Virchow's Archiv*, Band cxiv, p. 557. [2] *Ibid.*, cxliii, pp. 173 and 416.
[3] *Transactions of the Association of American Physicians*, 1905, xx.
[4] *Wien. med. Woch.*, 1875, xxv, 166. [5] *Inaug. Diss.*, Halle, 1889.
[6] *Arch. f. klin. Chir.*, 1892, xliii, p. 322. [7] *Ibid.*, 1877, xxi, Suppl., 157.
[8] Cases reported to 1897 have been collected by Glockner, *Zeit. f. Heilkunde*, 1897, xviii; to 1905 by Bloch, *Les Néoplasmes malins primitifs de la plèvre*, Paris, Vigot Frères.
[9] Two among 2000 autopsies at the Massachusetts General Hospital, a third and unpublished case of S. D. Wolbach's.

condition has not infrequently escaped detection because of the readiness with which it may be confused with chronic pleuritis, without a microscopic examination of the tissue. The disease is more common between forty and fifty years, but the ages of the reported cases vary from ten to seventy-four years. Men are somewhat more frequently affected. In rare instances it has followed trauma to the chest wall.

**Pathology.**—The disease is usually unilateral and occurs about equally on the two sides, although the right pleura has been somewhat more commonly involved. Rarely both pleuræ are invaded. The entire pleura of one side may be increased in thickness to 1, 1.5, or even to 2 cm. In other cases only a part of the pleural sac is diseased. The affected region is usually diffusely invaded, is gray or grayish yellow in color, and studded with discrete to confluent white, grayish or yellowish nodules, varying in size from a pinhead to a pea. More rarely the pleura is the site of larger multiple and isolated masses of growth. At times there are no nodules; the pleural surface is merely uneven and apparently diffusely involved. The tissue is hard and tough on section. Ulceration is not found. Adhesions are common. A variable amount of bloody, less commonly serous, rarely purulent fluid is usually present.

On microscopic examination the thickened pleura is found to be made up of aggregations of cells, of an epithelial character, and connective tissue, each in varying proportions in different parts of the sections. In places corresponding to the nodules seen on gross inspection, the tumor cells are closely packed together, forming small groups, separated by a thin stroma. In the intervening tissue and in places where the growth is more diffuse the stroma may predominate with scattered round, oval, or elongated groups of epithelial-like cells in alveolar arrangement, in few or many of which a lumen may be seen and a resemblance to tubule formation. Small areas of necrosis are occasionally present. The connective tissue is usually poor in cells, but in places is infiltrated with varying numbers of small round cells. The epithelium of the free surface of the pleura is usually absent over the whole or greater part of the sections, and in most of the cases has not apparently taken part in the new-growth. The bloodvessels, which may be increased in size and number, have likewise been uninvaded in most of the cases. The lymph vessels and spaces appear to be the principal site of the new-growth, and to many observers their endothelium its points of origin. An apparent transition from the flat cells lining the lymph channels to the larger polymorphous epithelial-like tumor cells, with vesiculated nuclei and variable amount of granular protoplasm, has frequently been noted. In some of the reported cases and in places in sections studied by the writer the groups of tumor cells partly or wholly fill lymph channels, the endothelium of which appears quite normal. Rarely, the surface epithelium of the pleura appears to have participated in the proliferation. In Benda's case[1] the pleural surface was beset with small nodules; on microscopic examination it presented a villous-like appearance, and he observed an apparent transition from surface epithelium to the tumor cells. It seems to the writer, however, quite impossible to judge whether the tumor cells arise from proliferation of cells already existing in the part or are invading the tissue through the lymph channels.

Metastases have been observed in the supraclavicular (Fränkel and

[1] *Deut. med. Woch.*, 1897, Nr. 21, p. 324.

Bonheim), the axillary glands (Neelsen), and the thoracic muscles (Neelsen, Perls, Pirckner, Glockner, and Schulz), spontaneously or along the needle track, after withdrawal of pleural fluid (Podack and Scagliosi). The disease has usually invaded other organs when death occurs. The most frequent site of secondary deposits is in the lungs. The bronchial, tracheal, mediastinal, retroperitoneal, and mesenteric glands, the viscera, other serous membranes, etc., may be the site of metastases. In six of the reported cases (Wagner, Böhme, Teixeira de Mattos, Benda, Scagliosi, and Bonheim) no metastases were found. In the presence of carcinoma elsewhere than in the pleura, and especially with the disease in the lungs, it is never certain that the pleural disease is primary.

**Symptoms.**—The disease usually begins like an ordinary pleuritis, and in its course closely resembles pleural tuberculosis. Pain is usually a prominent symptom and is often increased by a long breath and cough. Dyspnœa and cough are not usually striking features at first, but may be present without invasion of the lung. In the presence of pleural fluid, dyspnœa may be extreme and orthopnœa may be present. If the lung is involved the sputum may contain blood. Fever is usually absent. Loss of flesh and strength are usually progressive.

An accumulation of pleural fluid is almost constant and the physical signs are such as are commonly found with pleural fluid from other causes, although certain additional features may permit a probable diagnosis. The progressive loss of flesh and strength will naturally suggest a severe affection. The absence of signs pointing to disease in the apices of the lungs, the failure to find tubercle bacilli in the sputum, and the afebrile course may argue against tuberculosis; a negative tuberculin injection may positively exclude it. The presence of metastases in accessible regions may be an important sign. Inoculation metastases in the course of the needle track are especially important and suggestive and should always be sought in suspected cases. They are usually small, flat, hard, slightly movable, and painless. Invasion of the needle track with tuberculous material from the pleura may likewise occasionally give rise to similar nodules and thus their excision and microscopic examination may be necessary to establish the diagnosis.

On examination of the thorax, diminished expansion of the affected side may be a striking feature. During the early part of the disease the side may be more prominent, to appear somewhat smaller later, with relatively narrow and less depressed interspaces. With effusion, the heart may be displaced, returning at first to its former position after the withdrawal of the fluid. As the new-growth gradually invades a larger territory and as the pleura becomes thicker and less elastic, with the formation of adhesions, the heart often fails to return to a position which it might be expected to assume after the removal of such an amount of fluid. For similar reasons, the thoracic distress and sense of pressure are afforded progressively less relief from the evacuation of the fluid, which re-accumulates more rapidly. The operator may also be able to appreciate the much thickened and tough pleura by the resistance offered in the introduction of the trocar. The physical signs may show little if any change after the removal of even large amounts of fluid.

Examination of the pleural fluid may afford important data for diagnosis. It is often serous at first, becoming blood-tinged or even strongly hemorrhagic after the first or the first few tappings. This is due to the

inelastic character of the pleural walls, and probably, too, as examination of sections shows, to the not infrequent presence of bloodvessels near the free surface of the pleura, from which under the influence of increased negative pleural pressure following removal of the fluid, blood is readily extravasated. With the progress of the disease and the frequent repetition of tapping the fluid may resemble pure venous blood or have a chocolate color. That its bloody character is associated with the use of the trocar is suggested by the more frequent bloody character of the fluid in cases in which fluid has been withdrawn and the occurrence of serous fluid in cases which have been allowed to run their course without such interference. Careful chemical examination of the pleural fluid has not been made. The specific gravity, when taken, has usually been 1018 or under. Microscopic examination of the sediment may assist in a decision between malignant disease and tuberculosis. In carcinoma of the pleura there is usually a much larger proportion of endothelial cells, with a relatively small proportion of lymphocytes, the cytological formula thus conforming to that in fluids due to stasis. There is no reason to believe that the large cells, with vesiculated nuclei and vacuolated protoplasm, not infrequently found in plaques, are other than desquamated cells from the free surface of the pleura. In the writer's opinion there is no striking or constant difference between these large cells in cases of stasis and in malignant new-growths of the pleura. The glycogen reaction is found in cells from pleural fluid of other than malignant origin. The presence of many cells showing typical or atypical mitoses has been thought diagnostic of malignant disease.

It may rarely happen that the microscopic examination of a small piece of tissue removed with the needle may establish the diagnosis.

**Prognosis.**—The disease usually terminates fatally within six months of the discovery of the pleural invasion. A period of eighteen to twenty months may elapse between the beginning of symptoms and the fatal termination.

**Treatment.**—This is largely symptomatic. Removal of the pleural fluid usually affords only temporary relief. At times it has been followed by marked improvement, especially in the early stages of the disease. As the disease progresses, distressing pressure symptoms usually necessitate more frequent withdrawal, and not infrequently with less and less relief. At times, with much thickening of the visceral pleura, removal of fluid may only aggravate the symptoms from increased tension on a retracted and adherent lung. Morphine in sufficient doses is of value and may prolong the necessary intervals between the tappings. The repeated removal at short intervals of a very bloody fluid may hasten the fatal termination, but in consideration of the relief of distressing symptoms its evacuation seems justifiable if other means fail. It is better to withdraw small amounts frequently than to empty the cavity at each tapping. Free drainage of the pleural cavity by resection of a rib has been followed by a change in the character of the pleural fluid from bloody to serous.

2. **Sarcoma.**—Primary sarcoma is even less common than primary carcinoma in the pleura. Although in some of the reported cases a distinction has not been made between the two groups, this is justified from the general character and histological appearance. Thirteen cases are reported, and only 1 case has come under observation of the writer.[1] Nine of

[1] Twelve cases will be found referred to and summarized in Bloch's *Les Néoplasms malins primitifs de la plèvre*, Paris, Vigot Frères, 1905. Cases of Bernard, Blumenau,

these 14 cases occurred in males. The ages varied from seven to seventy-six. Of the remaining patients, 2 were from ten to twenty, 4 from twenty to thirty, 2 from thirty to forty, 1 from forty to fifty, 2 from fifty to sixty, and 1 from sixty to seventy. The two sides are about equally affected. In their clinical course they resemble primary carcinoma of the pleura. A collection of pleural fluid practically always accompanies the new-growth, and this is usually bloody, rarely serous. Its hemorrhagic character may first appear only after tapping. The presence of spindle cells in the sediment may suggest spindle-celled sarcoma of the pleura, as in Warthin's case.

In gross character at autopsy, primary sarcoma of the pleura usually presents a different appearance from primary carcinoma. In rare instances, however, as in primary carcinoma, the pleura may be diffusely and homogeneously invaded. Rarely, there are innumerable small nodules, but the new-growth is commonly single, hard, or soft, its surface smooth or lobulated, in color white, gray, or reddish, of variable and usually considerable size, even at times reaching that of a man's head. The pleura may cover the growth which appears to arise in the subserous tissue. In other cases no traces of pleura can be found, and the tumor itself forms the lining of the pleural sac, yet ulceration is uncommon. Invasion of neighboring organs by extension or metastases in the lungs, the neighboring glands, ribs, vertebræ, liver, spleen, or superficial parts of the body has occurred. In 3 cases no metastases were found. From their microscopic appearance the tumors have been classed as simple sarcoma, round, spindle-celled, fibrosarcoma, and myxosarcoma.

C. **Secondary Malignant Disease.**—Malignant disease of the pleura is more commonly secondary than primary. The tissue may be invaded by metastases from a primary malignant tumor in any part of the body, but pleural invasion is more common in malignant disease of the lung, mediastinum, thoracic wall, or stomach. Metastatic new-growths of the pleura do not usually produce a diffuse infiltration of the tissue. There are commonly several isolated nodules or masses and more rarely the pleura presents a generally nodular appearance. Pleural fluid may or may not be present, and this may be serous, but is more commonly bloody. In cases of pleural carcinoma secondary to the disease in the breast, the clinical picture, course, and termination may resemble primary carcinoma of the pleura.

Of 178 cases coming to autopsy at the Massachusetts General Hospital with carcinoma in various regions, 10 showed secondary deposits in the pleura. Of 10 cases with carcinoma of the breast, the pleura was invaded in 4. Of 58 cases in which the disease was primary in the stomach, only 3 showed pleural metastases. In this series, carcinoma of the pleura was also secondary to the disease in the thymus and ovary. Of 42 cases of sarcoma, primary in various regions, the pleura was secondarily invaded in 9.

## ECHINOCOCCUS DISEASE OF THE PLEURA.

**Etiology.**—Following the ingestion of the egg of *Tænia echinococcus*, the embryo, liberated from its shell in the stomach, may migrate to the pleura. The course pursued in reaching the pleura is uncertain, but the

Brunati, Dumarest, Hofmokl, Israël-Rosenthal (two cases), Kaufmann, Ménadière, Mlodziewsky, Percy-Kidd and Habershon, and Regnault. A thirteenth case is reported by Warthin (*Medical News*, October 16, 1897). The writer has had an opportunity of studying an unpublished case of H. A. Christian's.

more frequent infection of the right pleura suggests a migration by way of the portal blood stream or biliary channels to the liver, thence through the diaphragm to the pleura. Infection may also be direct or by way of the lymph channels or the systemic circulation.

**Special Pathology.**—It is convenient for purposes of description to divide cases into those in which the disease apparently arises within the pleural sac or the pleural tissues: (*A*) *Pleural Echinococcus.* The difficulty of distinguishing cysts of the pleura from those developing in their neighborhood and the frequency with which the latter lead to disturbances in the pleura, justifies a further division of cases into (*B*) *Parapleural echinococcus*, in which the primary infection has taken place in a neighboring organ, but in its growth the cyst encroaches upon and develops at the expense of the pleural space.

(*A*) **Pleural Echinococcus.**—(*a*) PRIMARY.—The exact site of the primary infection is uncertain, as cases come under observation with the cysts already developed to a considerable size. The number of cases in which the disease is primary in the pleura is small. In the combined statistics of Neisser and Madelung, among 1179 cases, echinococcus was primary in the pleura in only 18 (1.5 per cent.). The literature contains reports of 43 cases.[1] The right pleura was involved in 25, the left in 10; in 8 the site was not given.

The cyst is usually situated at the lower, but may be confined to the upper part of the pleural cavity. The local reaction leads to the formation of a connective-tissue envelope, which is usually very thin, but may be thick. Pleuritis is uncommon. Enlargement of the sac gradually compresses or displaces neighboring organs. Perforation may occur into the lungs with evacuation through the bronchi; or erosion of the ribs and intercostal spaces may lead to rupture through the chest wall. Both are rare. The cyst may become infected, and presents the appearance of an encysted empyema. The most common type is a single cyst or one sac containing daughter cysts (endogenous echinococcus). Rarely more than one cyst is found. A pleural cyst with multiple external budding (exogenous echinococcus) is described by Cary and Lyon, and an alveolar echinococcus (*Echinococcus multilocularis*), apparently primary in the pleura and with coincident or metastatic multilocular cysts in the lung, the diaphragm, psoas muscle, and brain is reported by Hauser. The localization of cysts in the peripleural tissue, between the costal pleura and the thoracic wall, is difficult to determine. Their separate consideration is hardly justifiable,

[1] Neisser, *Die Echinococcus Krankheit*, Hirschwald, Berlin, 1877, 17 cases; Madelung, *Beiträge zur Lehre von der Echinococcen-Krankheit*, Stuttgart, 1885, 2 cases; Maydl, *Ueber Echinokokkus der Pleura*, Wien, 1891 (cases 8, 9, 11), 3 cases; Theophil Rosenthal, *Diss.*, 1881 (quoted from Winzerling), 5 peripleural cases; Winzerling, *Ein Beitrag zur Casuistik des primären Pleurachinococcus, Inaug. Diss.*, Jena, 1892, 3 cases; Mosler and Peiper, *Nothnagel's Spec. Path. u. Ther.*, Band vi, 1 case mentioned; Ascoli, *Rendiconto della Società Lancisianà* (quoted from Orlandi), 4 cases; Vannini, *Bulletino delle scienze Mediche di Bologna*, 1896, p. 240, 1 case; Pasca, *Rendiconto Società Lancisianà degli Ospedali*, Roma, 27 giugno, 1896, 1 case; Orlandi, *Gazetta medica di Torino*, 1898, 49, 1 case; von Bókay, "Festschrift" in honor of Abraham Jacobi, New York, 1900, 1 case; Cary and Lyon, *Transactions of the Association of American Physicians*, 1900, xv, 1 case; Blechmaan, *Ueber primären Echinococcus der Pleura, Inaug. Diss.*, Kiel, 1901, 1 case; Hauser, *Primärer Echinococcus multilocularis der Pleura und der Lunge mit entwicklung multipler Metastasen im Gehirn*, Erlangen u. Leipzig, 1901, 1 case; Ransom and Willis, *British Medical Journal*, 1903, i, 302, 1 case.

as they probably represent cysts arising in the pleural or subpleural tissue, the development of which toward the lungs is prevented by dense adhesions.

(*b*) SECONDARY.—1. *By Metastasis.*—It is still an open question whether an echinococcus cyst, primary in the pleura, can give rise to metastases in other and remote parts of the body. It is likewise uncertain whether unruptured cysts in parts distant from the pleura can lead to secondary pleural invasion. The weight of opinion, however, is rather that multiple and isolated cysts are due to infection with more than one *Tænia echinococcus* embryo at the same or at different times.

2. *By Extension.*—Auto-infection through rupture of the mother cyst, the evacuation of daughter cysts into neighboring tissues and their further development is established for abdominal echinococcus. A similar secondary infection of the pleura from the rupture of pulmonary or hepatic cysts may take place, but pleural infection with bacteria usually precedes or so quickly follows the rupture that unless operation is undertaken, death almost always occurs within a variable and usually short period.

(*B*) **Parapleural Echinococcus.**—(*a*) *Intact Cysts.*—In this class may be included cases in which the disease develops in neighboring organs, but encroaches upon and grows at the expense of the pleural space. The cases comprise for the most part those in which cysts are present in the peripheral parts of the lung, the upper part of the liver, or the region between the liver and the diaphragm; and more rarely echinococcus disease of the mediastinum, spleen, or kidney. The clinical picture may be quite indistinguishable from primary pleural echinococcus. Subdiaphragmatic and especially hepatic cysts are most common and the diaphragm may be elevated to the second rib and even to the clavicle. In both the subdiaphragmatic and pulmonary forms of the disease the heart may be displaced laterally, the liver dislocated downward. The condition of the pleura in the presence of an echinococcus cyst in its neighborhood is variable and depends to some extent on the presence or absence of suppuration in the cyst. The visceral and parietal layers may be free, serous or purulent pleural fluid may be present, but partial or complete adherence of its layers is more common and more favorable, as rupture of the cyst may then fail to infect the pleura.

(*b*) *Perforated Cysts.*—According to Neisser's statistics, echinococcus disease of the liver breaks through into the respiratory apparatus in about 11 per cent. of the cases. Disturbances of the pleura from parapleural echinococcus are certainly more common than from the primary disease. Depending on the previous condition of the pleura and the character of the cyst contents, rupture is followed by free or encysted, cystic, serous, or purulent fluid. Suppuration is practically a constant feature. The perforation of an adherent pleura with invasion of the lung or bronchi is most common. Of 30 cases in Davaine's series only 9 ruptured into the pleura, 21 into the lung or bronchi. In Neisser's 60 cases the pleura was invaded in 16, the lung in 12, and the bronchi in 32. Hepatopleural or hepatobronchial fistulæ may result, and bile may be found in the pleural cavity or even be expectorated. An echinococcus cyst of the lung may likewise lead to free or encysted and usually purulent pleural fluid, following rupture. If the pleuræ are adherent the pulmonary cyst may evacuate externally. Rupture into the bronchi is, however, more common.

**Symptoms.**—In rare instances there may be no symptoms. In cases in which the disease is primary in the pleura the symptoms are usually

those of a slowly growing intrathoracic tumor. Cough may be absent or present, with scanty mucoid sputum from an accompanying bronchitis. Dyspnœa is usually present and is progressive. There may be pain with respiration, but this is not a striking feature unless pleuritis is present. Fever is usually absent. Emaciation is not common in uncomplicated cases. The perforation of pleural cysts into the lung is rare. Septic pneumonia and even abscess and gangrene may follow. If there is free communication with the bronchi, clear cystic fluid may be expectorated. In this or in evacuated pus, hooklets or bits of cyst membrane may be discovered. Rupture may occur through the chest wall, following atrophy of the intercostal muscles and erosion of the ribs. Spontaneous rupture is likely to occur if the cyst has suppurated. The perforation of parapleural echinococcus into the pleura is less common than into the lung. Rupture may take place without symptoms; in other cases the patient may be conscious of the rupture, which is followed by pain of a severe character, and if suppuration is present, as is commonly the case, there is chill and fever. Rupture may be spontaneous, or may be induced by exertion or trauma. If sinuses connect with the liver, biliary coloring matter may be expectorated. Hepatic echinococcus cysts may perforate the pleura and be evacuated through the lung without characteristic elements in the sputum in case the bile passages fail to connect with the cyst.

Urticaria may follow the rupture of pleural echinococcus into the pulmonary or other tissues or of parapleural cysts into the pleura. Severe symptoms of intoxication, even delirium, collapse, and death may likewise follow the rupture.

The duration of pleural echinococcus is difficult to determine. To judge from its growth in accessible regions it may take from six months to a year for it to reach the size of the fist. Symptoms may arise only after it has attained a large size.

On examination the signs are usually those of encysted pleural fluid. There is diminished expansion of the affected side, which is likely to be prominent, with obliteration of the normal intercostal depressions. The side may be dull or flat on percussion and in some cases it is possible to note an irregular or evenly curved arching of the upper border of dulness, the convexity of which is directed upward. The tactile fremitus and breathing are diminished or absent; the latter may have a bronchial quality. The voice sounds are diminished and œgophony may be present. The signs are likely to be atypical. Between the involved area and the lung there may be an abrupt transition on auscultation to normal vesicular breathing. In the presence of a large cyst fluctuation may possibly be made out, but the hydatid fremitus or quivering of jelly sensation has not been observed. The liver or spleen may be displaced downward, the heart to the right or left. The presence of echinococcus cysts elsewhere in the body may suggest a similar affection of the pleura.

**Blood.**—The presence of eosinophilia in the circulating blood may be confirmatory. Cabot collected 30 cases of hydatid of the liver, only 2 of which were negative. Of 20 cases in Welsh and Barling's series all but 5 exceeded the average in health.

**Diagnosis.**—Infection with echinococcus is rare in North America and Great Britain, and cases which occur are for the most part in foreigners. A previous residence where the disease is prevalent, and contact with dogs

used for herding sheep, may be suggestive. Positive data for diagnosis are furnished only by the discovery of scolices, hooklets, or cyst membrane. If perforation has occurred into the lung, such material may be present in the expectoration. An urticarial rash following thoracentesis is very suggestive. The examination of the fluid obtained by pleural puncture may furnish suggestive chemical features. It is usually clear, transparent, and varies from 1009 to 1012 in specific gravity. Sodium chloride is present. Albumin is usually absent or present only in traces. Traces of inosit, succinic acid, and grape-sugar may be found, and although suggestive, are not distinctive of the disease. In some cases the specific gravity is high and the amount of albumin considerable. If degeneration has taken place, cholesterin crystals may be found. If infection has occurred, it may mask the appearance of the fluid.

A resort to thoracentesis for the diagnosis of pleural or pulmonary echinococcus is attended by considerable danger, for perforation of the enveloping connective-tissue sac and the cyst membrane may result in the evacuation of the cyst fluid into the pleura or the lung if erosion of its substance has already occurred. As the perforated cyst membrane is subjected to changes of intrathoracic pressure with respiration or cough, the contained fluid may find its way between connective-tissue envelope and cyst membrane to the bronchi. Urticaria, symptoms of severe intoxication, with gastro-intestinal disturbances, faintness, collapse, delirium, and even coma, and death may result. Pulmonary or pleural suppuration or suffocation from mechanical obstruction by fluid or cysts may occur. Maydl reports 11 cases of pleural or pulmonary echinococcus in which a fatal result followed thoracentesis. When we consider the infrequency of the disease, this is a warning which cannot be safely disregarded. If the diagnosis can be made without puncture it is better to resort to operation without previous exploration. If thoracentesis is done, a small trocar (not a needle) is less dangerous; and if the case proves to be echinococcus, operation should be at once undertaken.

The pleural, pulmonary, or subdiaphragmatic site of the disease may be difficult to determine and the different forms may co-exist. In Patella's case[1] the diagnosis before operation was pleural, after operation hepatic, and at autopsy pulmonary echinococcus. Centrally placed pulmonary cysts may be without signs. The cyst is usually single and in the lower lobes, more commonly the right. When signs are present with a cyst in the peripheral parts of the lung the signs are usually the same as in pleural echinococcus. Pain is less often present, dyspnœa may be more paroxysmal, cough is likely to be more troublesome, and the sputum may be bloody. Rupture into the bronchi is more common in pulmonary than in pleural cysts. The differentiation is often impossible during life, and even at autopsy it may be uncertain whether the growth started in the lung or pleura. Subdiaphragmatic cysts which may be confused with the pleural or pulmonary form usually involve the liver at its upper part or the space between liver and diaphragm. In either case the diaphragm is elevated, the lung compressed, the heart displaced to the right or left, and the liver depressed. The clinical picture may then resemble pleural echinococcus, but the depression of the liver and the lateral dislocation of the heart are less marked. Cough may be absent and dyspnœa less troublesome. The greater vertical excursion of the lower pulmonary margin and the presence of the diaphragm

[1] Quoted from Maydl, *loc. cit.*, p. 71.

phenomenon, with subdiaphragmatic cysts, may be important differential signs. The distinction between an intrathoracic and intra-abdominal cyst is important for surgical interference.

Of pleural diseases, echinococcus may be confused with benign or malignant new-growths and encysted or free pleural fluid. Benign tumors are so rare as to need no special consideration. Aside from the history of opportunities for infection in echinococcus and the presence of cysts elsewhere, the differentiation could hardly be made. Of malignant disease, the secondary pleural carcinoma or sarcoma can usually be excluded by the presence of a primary focus elsewhere. In primary malignant disease the course is more progressively downward, with loss of flesh and strength. Superficial metastases may be found. Pain is a more prominent symptom. Owing to the diffuse character of the process, the whole or a greater part of one side of the chest may be dull. The percussion note is more board-like, and if free fluid is present its upper border may show a characteristic curve. In the later stages of malignant disease the affected side is more often somewhat contracted. If inflammatory fluid is present there is often the history of an acute onset with pain and fever. There may be evidence of pulmonary or other disease to which the pleural fluid is secondary. The pain is likely to subside as the fluid accumulates. Such processes seldom last as long nor does the accumulated fluid as slowly and steadily increase. With free fluid the line of demarcation between it and the lung, determined by auscultation and percussion, is less abrupt than in echinococcus disease, the upper limit of flatness may have a characteristic curve, and changes in level may be made out on changing the position of the patient. If encysted fluid is purulent, its character may be suggested by symptoms of sepsis. The appearance, chemical character, and microscopic examination of fluid obtained by puncture afford valuable data for differential diagnosis. Urticaria following exploratory puncture should suggest echinococcus disease.

**Prognosis.**—This is practically hopeless for cases of echinococcus cysts of the pleura or the parapleural tissue rupturing into the pleura, and allowed to run their course without treatment. Of 31 unoperated cases in Neisser's "statistics," including 12 pleural, 7 pulmonary with pleural perforation, and 12 hepatic with pleural perforation, all died. The prognosis is much worse for pleural than pulmonary echinococcus, in which perforation into the lung may be followed by recovery. The prospect in operated cases is much more encouraging. Of 13 operated cases of pleural echinococcus in Maydl's statistics, 4 (30 per cent.) died.

**Treatment.**—Evacuation of the cyst contents with the trocar, with or without the injection of solutions containing iodine or other substance, has been followed by cure, but is uncertain and too dangerous to recommend. The high mortality following puncture of the cyst has been mentioned. A radical operation only can be considered. Costatectomy is better than simple incision. If possible, the cyst should be removed without rupture. If too large to be removed entire, the cyst membrane may be drawn into the wound of operation and aspirated. It may then be shelled out from its capsule. As it is often difficult to be certain that the cyst is not pulmonary or subdiaphragmatic, the pleura should be carefully approached. If suppuration of the sac has taken place, the abscess should be opened and drained as in other suppurative pleural affections. Subdiaphragmatic cysts projecting into the thorax are best approached through the pleura.

# CHAPTER XXI.

## PNEUMOTHORAX.

By WALTER B. JAMES, M.D.

**Definition.**—The term pneumothorax is applied to cases in which air or other gas exists between the pulmonary and parietal layers of the pleura. The name pneumatothorax and pneumathorax have also been used in the past, but the one first given is universally made use of at the present time. It is not very common for gas to exist for any considerable time in this situation without the appearance of an exudate, and in these cases a prefix is used to signify the character of the fluid. When gas is present together with clear serum the condition is called hydropneumothorax or seropneumothorax. Where there is blood, it is hæmopneumothorax, and where pus, pyopneumothorax.

An attempt was formerly made to indicate which was the prior element in the anatomical condition by the order of the prefixes, calling it, for instance, pneumohydrothorax or pneumopyothorax to indicate that the appearance of gas in the pleura was the primary phenomenon. These latter titles have, however, been gradually abandoned on account of their clumsiness, and by reason of the great difficulty that is met with in establishing such priority. It is a fairly general custom and may be considered correct to speak of all cases in which the pleura contains gas as pneumothorax without reference to the question of the presence or absence of any other abnormal elements.

**Historical.**—In the writings commonly ascribed to Hippocrates, succussion and the sound produced by it are frequently mentioned, so that it is evident that the existence of the lesion was early recognized, but it was regularly confounded with empyema, the difference between the two conditions not being clearly understood for several centuries. From time to time cases were reported and descriptions were published, generally of the traumatic variety, until in 1803, Itard[1] published his dissertation on pneumothorax in which he was the first to formulate the knowledge of the subject, and showed that it so often occurred as a complication of the common pulmonary disorders.

In 1819, Laennec published the most important early account of the disease, in which he described exhaustively the nature and causes of the condition, together with the symptoms and physical signs, and this may be fairly considered the first successful effort to place in the hands of the profession a complete and accurate treatise on this disease. Emerson[2] in 1903 published an elaborate treatise on pneumothorax, by far the most exhaustive and complete that has yet appeared, in which he includes a complete review of

[1] *Dissertation sur le pneumothorax*, etc., *Thèse de Paris*, 1803.
[2] *Johns Hopkins Hospital Reports*, 1903, vol. xi.

the literature in detail, with a full discussion of the disease, its symptoms and signs in all of their relations, including an account of his own experiments on the physics of the chest. To this the reader is referred for complete abstracts of all the important literature to date, and for a detailed account of the facts that are known and theories that have been propounded. Since the publication of Emerson's treatise no new important light has been thrown upon the problems presented by this disease.

**Physiological.**—A knowledge of the essential features of the mechanics of the lungs and pleura is necessary to a clear understanding of the nature of pneumothorax.

The lungs hang free in the chest, and are kept everywhere in close apposition with it by atmospheric pressure exerted through the trachea, by reason of the fact that the chest is a closed and more or less rigid case, while the lung is a highly elastic and distensible structure, which may be regarded as hollow and in free communication with the atmosphere. In health, the force with which the pulmonary pleura is applied to the costal equals the pressure of the atmosphere minus the contractile force of the lung, which latter differs according to the state of distention of the organ, that is, with the stage of respiration.

It is customary to speak of the difference as the negative pressure of the pleural space, meaning thereby the pull exerted by the lung against the chest wall, but it should be remembered that this is not properly a pull, as in health the pulmonary pleura, not being adherent to the costal pleura, is not capable of pulling it. The so-called pull of the lung is in reality the push of the pressure of the atmosphere against the exterior of the thorax, and it is this that normally produces a depression of the intercostal space, pressure against the inner surface of the chest being equal to atmospheric pressure minus the elasticity or contractile force of the lung, which must be overcome before the two pleural surfaces can be brought in contact, and this force also aids in maintaining the normal position of the mediastinum, the diaphragm and the viscera occupying the upper part of the abdominal cavity.

It has long been the custom to speak of this contractile force or elasticity of the lung as negative thoracic pressure, and the term is therefore retained here on that account and because of its convenience. During life there is normally always such a negative pressure even in extreme expiration, that it is impossible to so nearly empty the lungs of air as to use up the entire contractility of the organ. The only circumstances under which the lung can exert an active pull upon the chest wall is when it is closely tied to it by pleuritic adhesions.

Whenever, owing to the presence of any foreign substance in the pleura, whether it be air, fluid, or a solid growth, the lung becomes smaller than normal, the contractile power and negative pressure correspondingly diminish. Many attempts have been made to measure the negative pressure of the chest by the use of a manometer applied to the pleura in living animals and in the human cadaver. After death the conditions change, and the results of such investigations can hardly be applied to the living men. The lungs naturally soon lose part of their elasticity, and, moreover, some of this quality may well depend upon the maintenance of the circulation.

It is also manifestly improper to apply the results in animals to human beings. Aron[1] found a healthy individual who was willing to lend himself

[1] *Die Mechanik und Therapie des Pneumothorax*, 1902.

to the trial of a manometer inserted in the chest, and in him he found, as an average of thirty-six observations, that the maximum reading for quiet inspiration was 5.09 mm. Hg, while the minimum for expiration was —2.54 mm. Hg.

It must constantly be borne in mind, however, that as the so-called negative pressure expresses only the elasticity of the lung, it may very well vary within wide limits among normal individuals, and, what is more important, it will naturally vary with the presence of any disease in the lung, and such variations may explain the wide difference in the clinical behavior of many cases of pneumothorax, as well as wide differences in their intrapleural manometric readings.

It would naturally be supposed that when the chest wall is opened, whether by accident or in the course of a surgical procedure, the lung would at once collapse, attaining the size and shape that it would take could it be removed entirely from the body and yet retain its living elasticity and contain its normal amount of blood. But it has long been noticed that when the chest is opened, either by accident or design, it sometimes happens that the lung not only does not collapse, but tends even to protrude from the wound, producing a hernia of the lung. This observation for a time hindered a clear understanding of the physics of the lung and chest wall, and encouraged a belief that the organ by its own inherent properties tended to expand and keep the chest cavity completely filled. Subsequently this phenomenon of hernia of the lung was explained by an assumed cohesion between the two pleural surfaces, which was said to be greater than the elasticity of the lung itself.

It is now generally admitted that the distention of the organ is produced by the powerful respiratory efforts acting upon the healthy lung, and thus raising the air pressure in the trachea and bronchi to a point exceeding the contractile force of the organ. This pressure, reaching the affected lung through its main bronchi, distends it and makes it not only fill its chest cavity but even protrude through the orifice in the wall.

**Incidence.**—The largest number of cases occur in early adult life, probably because it is at this time that pulmonary tuberculosis is most common and most rapid in its course. Angel Money mentions a case at three months and Ormerod one at six months. It is more common in men than in women, probably because the former are subjected to greater physical exertion. Of the writer's 125 cases collected from three hospitals, 103 were in males and 22 in females. It is more common on the left than on the right side. In 85 of this series it occurred on the left side in 49 and in 36 on the right.

**Etiology.**—The presence of gas may be brought about in three ways: First, by a penetrating lesion of the chest wall, opening a communication with the outside air or with a gas-containing organ, and so admitting air or other gas into the pleura. Second, by a lesion of the lung producing a similar communication between the atmosphere and the pleural space through the bronchi. Third, by the decomposition of a pleural exudate with the formation of gas.

In the first two of these groups, the contained gas is generally atmospheric air, which may be subsequently changed in its character. In the third it is a gas, the composition of which will depend upon the nature of the microorganisms which bring about the decomposition.

Traumatic pneumothorax may be brought about by any penetrating

wound of the chest wall or lung. It is common in stab or gunshot wounds of the thorax, and every case of empyema that is operated upon in the ordinary way becomes an open traumatic pneumothorax. It may be due to the perforation into the pleura of a lesion of one of the abdominal viscera, as from abscess of the liver, cancer of the stomach, cancer of the œsophagus, ulcer of the stomach, abscess of the vermiform appendix, and hydatids of the liver.

In fracture of the ribs a sharp fragment of bone not infrequently injures the lung and so produces pneumothorax. Among 127 cases, 11 were from this cause. Hæmopneumothorax is especially likely to be present in this group. Occasionally in severe accidents with marked concussion of the body there is rupture of the lung and pneumothorax, without an external wound or fracture of a rib. Traube reports such a case of pneumothorax following severe general concussion of the body, in which no fracture of a rib could be made out.

An interesting form of lung injury is that which occasionally results from penetration by the needle in thoracentesis. When we consider, however, how often the lung is wounded in this procedure, and how frequently the pleura is scratched and bleeds from violent coughing at the end of the operation, it seems remarkable that the accident occurs as rarely as it does, although it is possible that, as suggested by Ewart, it might be discovered more often if the chest were systematically searched soon after each tapping. Among 127 cases, 5 were from this cause. Several cases have been collected by Sears, where through carelessness in arranging the valves, in the attempt to aspirate the fluid in serofibrinous pleurisy, air was pumped into the chest, thus producing pneumothorax.

Pneumothorax may result from the spontaneous perforation of an empyema either through the lung or through the chest wall, empyema necessitatis, but the former mode of origin is extremely rare, probably because, in the first place, it is difficult for pus to find an exit and air to find an entrance through such a small opening at the same time, and also because such empyemata are generally of long standing, with much thickening of the pleura and with many adhesions.

In rare cases pneumothorax has resulted from echinococcus disease of the lung, generally late in the malady and where pneumonic consolidation has resulted and has undergone necrosis and softening with rupture into the pleura, thereby simulating the method of production in tuberculosis. It may result from breaking down of any tumor of the lung, or from tearing of the adhesions associated with such tumor. In only one of the writer's series was this the cause.

The commonest cause of pneumothorax is disease of the lung, and the most important of these diseases is tuberculosis. It is impossible to establish the proportion of the cases of pneumothorax which are due to tuberculosis, but it is certain that the great majority belong to this class. Weil reported 55 cases of the disease, of which 46 were due to tuberculosis, while other authors have reported even higher percentages, and it is generally believed that about 90 per cent. of all the cases are due to this. In the writer's series of 127 only 67 were recorded as due to tuberculosis. The marked difference in the statistics of the various authors upon this point may be due either to differences in the character of the hospital service from which the figures are taken, or, more important still, to difference in the individual point of view toward the diagnosis of tuberculosis.

It is also difficult to determine the proportion of cases of pulmonary tuberculosis that suffer from this complication. Weil found it in 10.1 per cent. of his fatal cases of phthisis, while West found it in 5 per cent., and Chambers in only 3.7 per cent. Drasche[1] has collected 10,212 cases of pulmonary tuberculosis, among which there were 198 of pneumothorax (1.93 per cent.). Of these 158 were in men and 40 in women.

It occurs most often in active cases of phthisis in which softening and cavity formation are going on, and is excessively rare in arrested tuberculosis, although one must consider many of the cases of so-called spontaneous pneumothorax, occurring in previously healthy persons, as probably due to the stretching or tearing of a pleuritic adhesion, which itself is often due to a slight subpleural tuberculous lesion which has healed. Its infrequency in the chronic miliary form of the disease is probably due to the fact that in these cases dense and more or less generalized pleuritic adhesions develop, which always render the occurrence of pneumothorax less probable, and sometimes impossible through obliteration of the pleural space.

For the same reason the perforation is only rarely situated at the apex, this being the commonest seat of pleuritic adhesions. It seems to occur rather more frequently on the left than on the right side. In 96 of the writer's cases, 55 were of the left side and 41 of the right. According to Fränkel, cavities of large size rarely rupture, this occurring more often in softening foci of small size situated immediately beneath the pleura; he regards the location of a focus as of much more significance in relation to possible rupture and pneumothorax than its size or character.

It has long been supposed that a violent effort, as lifting, coughing, or sneezing was often the immediate cause, but such an effort is certainly not necessary, as many cases occur when patients are at rest, or even in the night while sleeping.

Finally, there are the so-called spontaneous or idiopathic cases of pneumothorax. In these the condition comes on suddenly in a person previously healthy. It may follow some unusual exertion, or may come on when he is at rest. Thus, in a young man, an electrician, pneumothorax suddenly developed while he was standing on a ladder in a strained position, and reaching with both hands above his head. He had been previously in perfect health, and his rapid and complete recovery made it seem unlikely that he had any serious organic disease of the lung. In another case, an elderly gentleman, apparently sound and in perfect health, developed pneumothorax of limited extent. The only cause that could be discovered was a habit which he had cultivated, as part of his morning and evening calisthenics, of violently beating his entire body, especially the chest, with closed fists. He consulted a physician on account of a vague sense of discomfort in the right side and somewhat troublesome dyspnœa on exertion. Cases have been reported in which the accident followed laughing, crying, coughing, sneezing, yawning, or in a paroxysm of coughing in whooping cough.

Fussell and Riesman,[2] who tabulated and studied 58 cases, find that it is most common in young men; 3 cases that have come under personal observation were all men; 2 were below forty and 1 was sixty-two.

[1] *Wiener klin. Woch.*, 1899, p. 1117.
[2] *American Journal of the Medical Sciences*, August, 1902.

The mechanics of the development of these spontaneous cases has long been a matter of dispute, but it is now generally believed that they are, as a rule, the result of tearing or stretching of the lung where it is bound down by pleuritic adhesions. It has long been claimed that it may be produced by the bursting of an emphysematous vesicle situated on the surface of the lung. Fränkel finds that it occurs less often in true pulmonary emphysema than in the interstitial type, and that it most often results from rupture of a subpleural vesicle. Neither of these hypotheses is susceptible of direct proof, as this form of the disease almost never proves fatal, but the weight of opinion lies in favor of pleuritic adhesions as the probable cause in the majority of cases.

**Pathological Anatomy.**—The pathology of pneumothorax is simple. The air which finds its way into the chest is either free from bacteria, as is generally the case in spontaneous pneumothorax and occasionally in tuberculosis, or it may convey pathogenic bacteria, as when the communication is with the open air, or is made through a focus of infection in the lung. When the communication is with one of the abdominal viscera, there is even greater likelihood of the admission of bacteria.

In the first place the condition may remain a pure pneumothorax, there being no serous exudate that can be discovered by physical examination or by puncture. This is especially true of the spontaneous cases, where the amount of air in the pleura may be small and confined to a limited area. This is probably due to the fact that the lung lesion is of slight extent, and, being at the periphery, there is no communication directly with a bronchus, but only with alveoli, so that the fistula is readily closed. It has been assumed, also, that the perforation in the lung is soon sealed by an inflammatory exudate. If no more air finds its way into the pleura, that which is present soon loses its oxygen through absorption into the blood, the nitrogen being more slowly taken up, until after a period varying from a few days to several weeks, all signs of pneumothorax have disappeared, leaving the chest normal.

Occasionally, a serofibrinous pleurisy develops, with a fluid exudate in the chest, thus producing hydropneumothorax, but whether a bacterial infection is necessary to the development of such a pleurisy cannot be positively stated. It was assumed by Wilson Fox that in such cases of hydropneumothorax there was a preëxisting irritability of the pleura. It has been estimated that only about 10 per cent. of all the cases of pneumothorax remain free from exudate.

When there is no infection and no fluid, the pleura remains normal. The lung collapses to a varying degree, dependent upon the amount of air that is admitted into the pleural cavity, and upon the freedom of the pleura from adhesions.

The perforation itself varies much in character. There may be a ragged hole, easily discovered, admitting the finger into a tuberculous cavity, or the aperture may be so small and so hidden as to be invisible, or discoverable only upon submerging the organ in water. In some cases the opening has become completely plastered over by inflammatory exudate, the patient having then a closed pneumothorax without communication with the external air.

It was formerly supposed that the presence of air in the pleura always set up an inflammation of the membrane, but experiments upon animals

and further study of human cases have shown that this is not true, and that, on the contrary, air as such does not act as an irritant to the pleura. When inflammation does follow it is due to some additional cause, generally an infection. In the 58 cases of spontaneous pneumothorax collected by Fussell and Riesman, only 1 showed a pleural exudate.

In hydropneumothorax the pleura presents the same anatomical changes as in pleurisy with effusion, while in pyopneumothorax the changes are the same as in empyema. In hydropneumothorax the pleural surfaces are coated with fibrin, the pleura being the seat of an acute exudative inflammation. In the purulent form, if the disease lasts a considerable period, the pleura is much thickened through the formation of granulation tissue, which completely changes its structure, and is covered with a layer of fibrin and pus. In cases of longer duration the thickened pleura may undergo calcareous degeneration, while the adjacent structures of the chest wall may become the seat of a chronic inflammation, giving rise to periostitis, perichondritis, and even caries or necrosis of the ribs. In some cases the pus becomes fetid.

In pneumothorax displacement of the thoracic and abdominal viscera takes place, often to a remarkable degree, but in proportion to the amount of air and fluid that are present. The affected lung is shrunken and compressed backward and inward, and may even lie along the spinal column as a tough, fibrous mass of tissue containing almost no air, and presenting no resemblance to the normal lung. It generally shows tuberculous areas and often a cavity of considerable size.

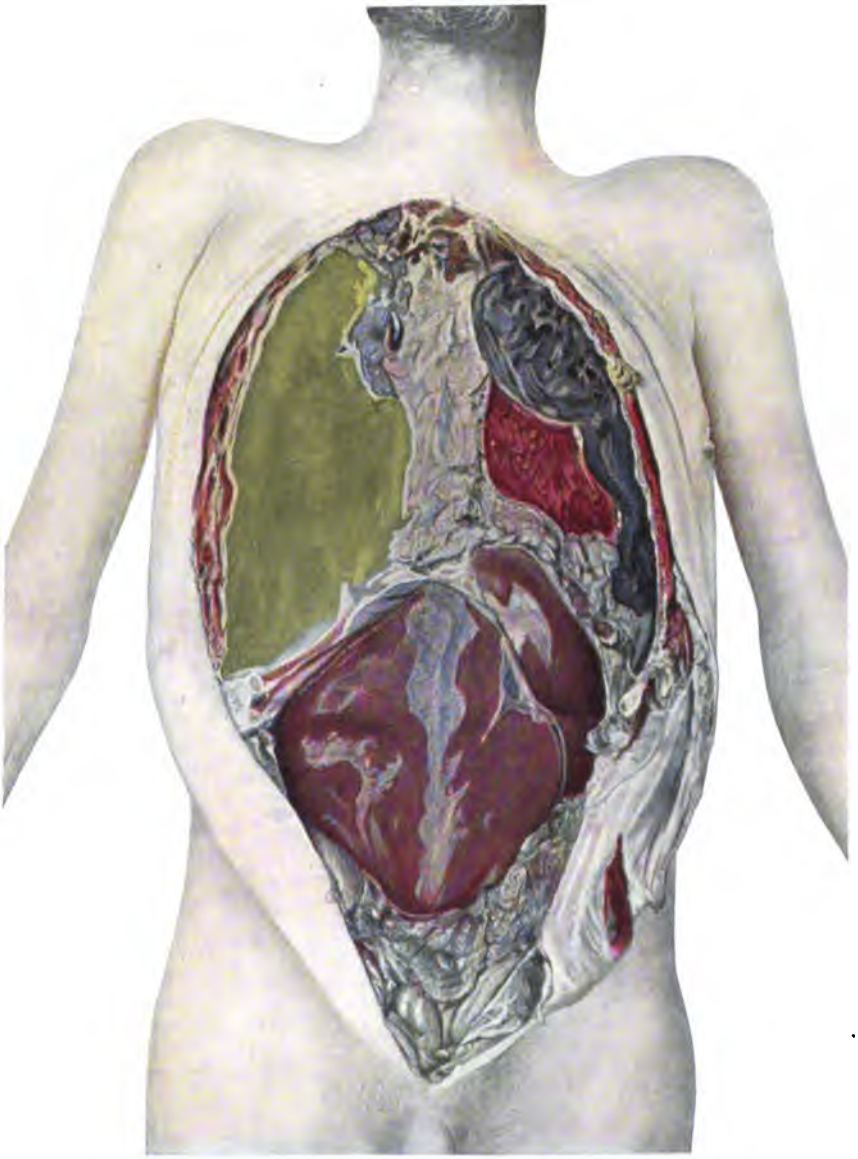
The affected side of the chest is generally increased in size, the increase being most marked in the lower portion. The mediastinum is displaced toward the healthy side, with all of its contents. This displacement is most marked in left pneumothorax, in which the heart may lie entirely to the right of the middle line. Contrary to the general impression, the heart is not rotated or swung from its point of attachment at the root of the great vessels, but is moved bodily across to the opposite side, its long axis maintaining about its normal relation to the long axis of the body. Thus the visible and palpable cardiac impulse does not represent the situation of the apex of the heart, but of the upper and anterior portion of the right ventricle.

The opposite lung is crowded outward and backward, and its compression may add materially to the gravity of the situation. In pneumothorax of the right side a corresponding displacement of the mediastinum to the left takes place, but to a less extent. (See Plate V.)

The diaphragm suffers a remarkable change, being crowded downward, encroaching upon and displacing the abdominal viscera. When in addition to the gas a large quantity of serum or pus is present, the vaulting of the diaphragm is reversed so that it projects downward, presenting its convexity in the abdomen, where it may be plainly seen in fatal cases when the anterior abdominal wall is first opened. This gives rise to what has been called "the paradoxical contraction of the diaphragm," as described by Ewart[1] in 1890. This has been studied by the use of the *x*-rays, and shows a rise of the surface of the fluid with inspiration and a fall with expiration. This reversal of the normal position and action of the diaphragm is due to the

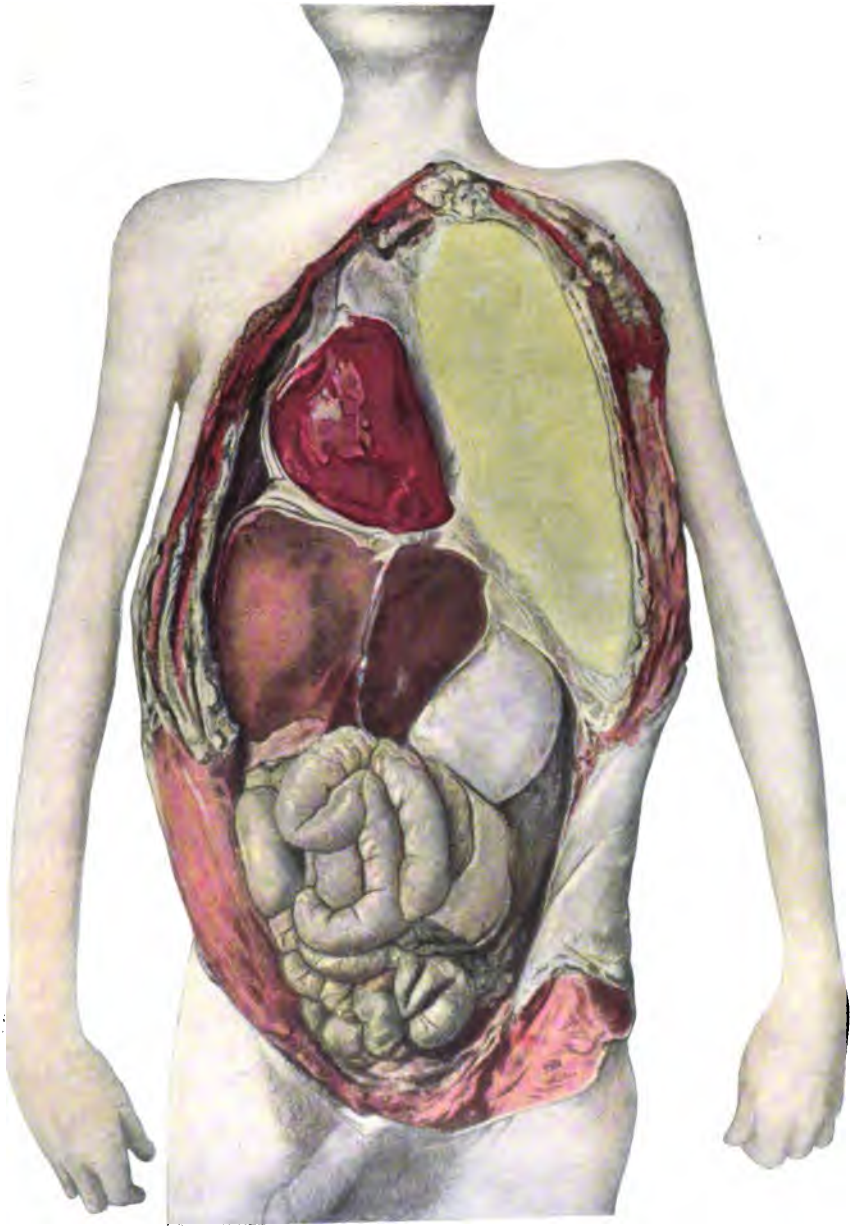
[1] *Transactions of the Medical Society of London*, 1890, xiii, p. 56.

PLATE V



Pyopneumothorax—Right Side

PLATE VI



Pyopneumothorax—Left Side

fact that in health its shape is maintained partly by the contractile force of the lung. When air is admitted to the pleura this force becomes inoperative as far as the diaphragm is concerned, and the latter then sinks. If there is only air, it takes approximately a horizontal position. If a considerable quantity of serum or pus is present, it is forced downward by the weight as well as by the pull of the abdominal viscera, and projects into the abdominal cavity.

Under these circumstances some remarkable changes take place in the anatomical relation of the abdominal viscera. In right pneumothorax the liver is pushed downward and rotated to the left, this displacement often being very great, the lower right corner of the organ lying in the middle line below the umbilicus, and the upper surface occupying a large part of the anterior abdominal space, the stomach being crowded backward and completely covered by the liver. The spleen is crowded backward and to the left, the omentum and colon downward almost to the pelvic brim. When the disease is in the left chest and is extensive, the spleen is pushed downward and the stomach, colon, and liver far to the right side. (See Plate VI.) All of these anatomical changes are well shown in the accompanying plates made from photographs taken at autopsy. (See Plates V and VI.)

**Symptoms.**—Pneumothorax may develop either gradually or rapidly, and the symptoms of its onset will depend largely upon the extent to which it interferes with respiration. Occasionally, although rarely, pneumothorax is the cause of sudden death.

Where the affected lung has previously added much to the respiratory efficiency and where it is free to retract, because it is not the seat of extensive disease and is not bound down by pleuritic adhesions, the onset is sudden and striking. There is complaint of sudden sharp pain in the side, and of an immediate intense feeling of suffocation. The patient starts up in bed gasping for breath, the face is dusky and cyanosed, while the violent action of the accessory muscles of respiration testifies to the keenness of his distress. The alæ nasi are in active agitation, and he is either unable to speak or may plead to be taken to the open window. The pulse is rapid, small, and feeble, and may become imperceptible. The hands and feet grow cold and blue, the body becomes bathed in cold sweat, the temperature at first falls below normal and later rises, and the patient at first may resemble one suffering from thrombosis of the pulmonary artery, or the condition may suggest perforation of one of the abdominal viscera, with extensive shock. Occasionally repeated attacks of urticaria occur soon after the onset.

Sometimes the patients are conscious of the sudden tearing or perforation of the lung, or its rupture may even be heard. Occasionally the sudden stabbing pain, especially if on the left side, with dyspnœa, pallor, and a sense of impending death with inability even to speak, may make a picture closely resembling angina pectoris. Gaussier in 196 cases of pneumothorax reported 68 with sudden onset. Pulmonary tuberculosis of moderate extent and spontaneous pneumothorax furnish the largest number of cases with sudden and severe onset.

The aperture in the lung may be valvular, admitting air freely into the pleura, but blocking its return. Thus the violent respiratory efforts acting upon the other lung force air into the pleura until this becomes overdistended, displacing the diaphragm and compressing the sound lung. In these cases the dyspnœa and cyanosis become more and more urgent, and the patient

dies unless relief is speedily given. This is called valvular pneumothorax or suffocative pneumothorax.

Where the lung has been extensively diseased or bound down by adhesions, the onset is apt to be less rapid and urgent. There may be complaint of slight pain or of an increase in the dyspnœa already present, or it may be merely noticed that the patient seems more ill. In still other cases there may be no additional complaint made, no new symptoms, and the pneumothorax may be discovered accidentally in the course of the physical examination.

In spontaneous pneumothorax the onset is generally with pain and urgent dyspnœa, but occasionally the symptoms may be slight, only a sense of uneasiness in the affected side with moderate dyspnœa on exertion, the patient's occupation at no time being seriously interfered with. When it results from preëxisting disease in the abdomen, the onset of the pneumothorax may be marked by no striking symptoms, owing to the seriousness of the previous condition, or it may begin suddenly and severely. There are no prodromal symptoms that will enable one to anticipate or foretell the attack.

In milder cases the only symptoms that persist may be pain or uneasiness in the chest and dyspnœa on exertion, and these may not be severe enough to prevent the individual from continuing his vocation.

In severe cases the pain and dyspnœa persist or may grow worse, and the patient is confined to bed. The respiration is rapid, the pulse rapid and feeble, and the orthopnœa and cyanosis continue. Cough is often added, or may have already been present as part of the original disease. The heart's action remains rapid and then becomes feeble, and the peripheral circulation is but poorly maintained.

Valvular pneumothorax is an important variety in that its symptoms become at once alarming, the distress is very great, and death rapidly ensues unless relief is given. It occurs almost exclusively in pulmonary tuberculosis, and generally in advanced cases with extensive disease of the lung. After death a fistula of considerable size is generally found, the closure of which is often prevented by pleuritic adhesions. Air thus finds its way more readily into the chest than out of it, and through the violent respiratory efforts, intrapleural tension rises, with the patient's distress becoming greater and greater. Aron (Berlin, 1902) had the opportunity of studying experimentally the air pressure in a case of this form of pneumothorax by inserting a cannula connected with a manometer. During the period of marked dyspnœa he found the pressure at the height of inspiration +7.93 mm. Hg. In expiration it was +10.48 mm. Hg. He then opened the cannula and attempted by siphonage to remove the air, but was able to lower the intrapleural tension only to +2.85 in inspiration and to +3.39 in expiration. He never succeeded in lowering it to zero. This he believed was owing to the fact that the area of the opening in the lung was greater than the cross-section of the cannula, so that air could not escape as freely as it could enter the chest. By closing the cannula intrapleural pressure gradually rose again.

**Physical Signs.**—It is difficult for the physician or student of to-day to realize the eagerness and enthusiasm with which the physical signs were studied in pneumothorax and in many other thoracic diseases in the early part of the last century. Physical diagnosis in the modern sense had just been discovered, and had become an important chapter in medicine, and attempts were made to draw the subtlest distinctions between the various

conditions found in the chest in pneumothorax, and to demonstrate differences in the lesions that are now more readily and quickly and precisely made out through the aid of newer methods, such as bacteriology, exploratory puncture, etc.

Moreover, further study of the disease and careful comparison with postmortem records have shown in a general way that the finer shades of differences in the signs are not so precise and trustworthy a guide to the actual physical condition as was supposed. Yet here, as in so many instances in medicine, the pendulum has swung too far, and more time and care might well be given to the study and recording of physical signs than has generally been the case in recent years.

**Inspection.**—As a rule the patients lie most comfortably on the opposite side, but occasionally the knee-chest position is preferred, while sometimes a sitting or half-sitting posture gives most relief. After effusion has taken place the semirecumbent position or lying on the affected side is generally preferred. The respiration is almost always rapid and labored, while the distressed countenance, the cyanosis, and the free sweating all testify to the urgent sense of suffocation which is experienced. Often this is so extreme that speech is impossible.

When the pneumothorax is of limited extent, whether this is because the lung is the seat of extensive disease and therefore incapable of considerable retraction, or because its collapse is hindered by pleuritic adhesions, there may be no visible evidence of the existence of air in the pleura. Where the pneumothorax is extensive, however, and especially where a valvular aperture exists, with heightened intrathoracic pressure, the signs on inspection are striking. Yet since the work of Bard much doubt has been cast upon such heightened intrathoracic pressure as the cause of distention, Bard having found that no case of pneumothorax has been recorded in which the pressure was measured and found to be greater than 9 mm. of Hg., which pressure, he claims, is too slight to produce active bulging of the chest. It has been mentioned above that Aron in 1902 found the highest pressure measured in his case was +10.48 mm. Hg.

It is more reasonable to assume that the normal symmetry and outline of the chest, with the normal condition of the intercostal grooves, are maintained in great measure by the negative pressure produced by the contractile force of the healthy lung against the chest wall, that is, by excess of extrathoracic air pressure over intrathoracic, and that in pneumothorax these pressures are equal and so balance one another, the thorax then tending to take the shape and position it would occupy were it entirely emptied of lungs and left freely open. The normal depression of the intercostal furrows may disappear or even give place to bulging.

**Mensuration.**—Measurement may show the affected chest to be larger in circumference than the other side, but occasionally when on inspection the diseased side appears larger, measurement shows that there is actually no difference, or even that the normal side is the larger in circumference.

Subcutaneous emphysema is a fairly common accompaniment of traumatic pneumothorax, and not infrequently complicates the form which results from thoracentesis.

The displacements of the various viscera have been discussed previously, and these are valuable aids to the physical diagnosis of the condition.

It is rare in any other disease to find such extreme displacement of the

heart, especially when the pleural disease is on the left side, while the extreme displacement of the liver downward and the bulging of the diaphragm into the abdominal cavity all help to suggest the nature of the complaint. In spite of the often extreme displacement of the upper abdominal viscera, this feature is of less service in diagnosis than would be expected, for with the urgent dyspnœa the abdominal wall is generally so rigid that accurate determination of the size and position of these viscera is impossible.

An extreme but not infrequent displacement of the liver is seen in Plate V. In this case both fluid and air were present in very large quantity, but this same displacement has been reported by others in cases of simple pneumothorax without fluid. Sometimes the diaphragm can be found projecting below the costal margin.

In pneumothorax of considerable extent, movement of the affected side of the chest is lessened or may be entirely absent; this phenomenon is not to be distinguished, however, from the similar appearance present in extensive pleural effusion.

**Palpation.**—The palpation signs are not uniform, but are of some value in diagnosis. Most often vocal fremitus is diminished over the affected portion of the chest and sometimes it is absent. In rare instances it may be exaggerated.

In 70 of the writer's cases in which the vocal fremitus above the level of the fluid was noted, it was diminished in 52 and in 18 it was absent. When fluid is present, vocal fremitus is regularly absent below the level of this.

**Percussion.**—The percussion sound is probably to a large extent determined by the character of the chest wall, and especially by its tension. Percussion over the pneumothorax is often deceptive and uncertain, the sounds differing much in different cases, and often the physical grounds for such difference are undiscoverable.

Most often the note is hyperresonant, and sometimes it may be a true tympany, but not unfrequently the resonance is of the normal type, or there may even be dulness. These various percussion sounds may be obtained in cases which are of the same general type, and where no ground for the striking difference can be found, so that it seems most probable that they depend upon subtle variations in the sounding-board properties of the chest wall, depending upon size, shape, tension, etc.

The condition of the pleura probably has little influence in determining the percussion note unless it is so changed as to add very materially to the thickness of the chest wall. The percussion note is often modified by the presence of the retracted and condensed lung.

In general pneumothorax, as a rule, the lung lies along the spine in the posterior position of the chest, and is not susceptible of demonstration by percussion; but when it is the seat of extensive disease, or is held down by adhesions, its presence may be determined by impairment of the note, that is, by disappearance of hyperresonance over this area. Most often such signs are present over the apex, this being the commonest seat of adhesions. Occasionally the cracked-pot sound is heard, which may be the case either when there is a large, free opening in the lung communicating with the chest cavity, or when a lung cavity of considerable size lies close to the chest wall. Bäumler calls attention to the occasional existence of islands of tympanitic resonance below the level of the fluid, and suggests that they may be due to pleuritic adhesions.

The percussion boundaries of the chest are increased, bringing about a diminution or entire disappearance of splenic dulness if on the left side and of liver dulness if on the right, while cardiac dulness also disappears or changes its position. The percussion note may vary over different parts of the chest, and may also change with change of position or after aspiration. In most cases the tone becomes deeper on sitting up, becoming higher in pitch on lying down, this change being supposed to result from a lengthening of the longest diameter of the chest in the first case, due to the depression of the diaphragm by the fluid, and a shortening of it in the second case. This phenomenon is known as Biermer's change of tone, but it is not present in every case, and occasionally exactly the opposite has been noted. An elevation in the pitch of the percussion note on opening the mouth was supposed by Gerhardt to indicate an open pneumothorax, and the sign has since then borne his name, but it is not one upon which absolute dependence can be placed. This is practically the same as Wintrich's phenomenon as observed in open cavities.

The presence of a small amount of fluid in pneumothorax cannot generally be discovered by percussion. Where large quantities are present a flat note is generally obtained over this area, although even here the note may still be hyperresonant, but a smaller quantity may lie so low in the hollow of the diaphragm as to elude discovery. Generally, the fluid can be discovered by succussion long before its detection is possible by percussion, and in any case the physical signs give but a feeble clue to its quantity. It is a familiar experience of the autopsy-room to find considerable quantities of fluid in cases of pneumothorax that have been supposed to be dry, and most clinicians have been surprised on being confronted with large exudates which had either escaped diagnosis, or at least whose size had not been recognized. It was a famous observation of Skoda that it was safe to double one's estimate of the exudation in pneumothorax, as made from the study of the physical signs, but this rule is one that applies also fairly well in pleurisy with effusion. Moreover, it is not always possible to determine absolutely the level of the fluid, which is generally higher than it appears to be, and it often happens that a needle inserted for the purpose of withdrawing the gas is found to be below the surface of the exudate.

In pneumothorax more than in any other disease of the thorax the level of the fluid changes rapidly and completely with change of position, and this proves a striking contrast with what happens in pleurisy with effusion where the position of the exudate changes but little or not at all. Occasionally a helpful diagnostic sign is obtained by letting the patient lie on the healthy side, when a horizontal line of dulness can be made out at a varying distance above the spine on the diseased side. In cases where the lung fails to collapse, or where it is bound down by adhesions, these various percussion signs may become of much value.

Emerson has described two interesting cases in which a very large amount of fluid was present, with but a comparatively small quantity of air, so that instead of a large cavity with a moderate amount of fluid moving about in it there was a cavity almost filled with fluid and with a bubble of air which always sought the uppermost part of the space, and could there be discovered by physical examination.

**Auscultation.**—(*a*) The *respiratory murmur* is regularly changed in pneumothorax, but the changes are not always the same, nor can a safe conclusion

be always drawn as to the condition of the pneumothorax cavity from the characteristics of the sounds heard.

In a good many cases the respiratory murmur is diminished, and occasionally it is absent. The latter gives rise to many errors in diagnosis, but should always suggest pneumothorax when it exists over an area of the chest that gives exaggerated or tympanitic resonance. Tolerably often the first impression received is that of absence of respiratory murmur, but on keeping the ear applied to the chest and securing a quiet environment, a barely perceptible sound is heard, of amphoric quality, so feeble that it has been called the shadow of a sound. This condition existing over a cavity reminded Walshe of Shelley's line, "When night makes a weird sound of its own stillness."

Amphoric respiration is the variety most characteristic of pneumothorax and the mode of its production has been the subject of much discussion and dispute. While in most cases the phenomena of auscultation are difficult to discuss and compare, from the fact that they do not admit of imitation or reproduction, or even of clear description, yet the amphoric sounds are so striking and so unique that they can be recognized and defined, with the assurance that the phenomena being discussed by different observers are the same.

It should be borne in mind that the term amphoric describes only a sound quality, and that it has no relation to pitch, intensity, or duration, nor to the relation of inspiration to expiration; so that there may be amphoric breathing so loud that it can be heard without the ear to the chest, or so feeble that it can be heard only by a perfectly trained ear, and then only by the strictest attention. Laennec believed that it was essential to the production of amphoric respiration that a fistula opening into the cavity existed, through which the air might pass freely, and that the peculiar sound was produced by such passage of air in and out of the cavity. Others claim that the amphoric quality is added to the respiratory sound through the action of the chest as a resonance chamber, and that it is not made by passage of air through a fistula. It has been heard in cases which exhibited no such fistula after death, and, indeed, cases have been noted where the respiratory murmur acquired amphoric quality from an adjacent stomach or colon distended with gas. Careful sifting of the evidence indicates that while the sound may be produced at a fistulous opening, yet even here the peculiar quality is obtained from the cavity whose walls act as a sounding board, while it may certainly be produced in a pneumothorax cavity which is entirely closed.

Emerson describes the condition as follows: "The pneumothorax cavity, if it is productive of loud, amphoric breath sounds, does so through its properties as a resonance chamber, and by harmonic vibration will intensify those sound waves of proper wave length, and by its selective action in responding to certain over tones and not to others will change the quality of the sound."

The fact is, the chest possesses many of the characteristics of a musical instrument, and modifies sounds produced in or near it according to the laws governing sound production in such instruments. Amphoric breathing, then, is tolerably characteristic of pneumothorax, although not entirely confined to it, for it may also be heard over large cavities in the lung. In pneumothorax it is not heard uniformly over the diseased side of the chest, but is often limited in its area, while it varies also in intensity and pitch.

The heart sounds occasionally have the same metallic quality as that of amphoric breathing, deriving this from the adjacent cavity.

In 90 of the writer's cases in which the character of the respiratory murmur is recorded it was found to be as follows: amphoric in 31, diminished in 41, absent in 12, and bronchial in 6.

(*b*) *Vocal resonance* sometimes has an amphoric quality; this seems to follow the true voice sounds, and therefore is called amphoric echo. Such an amphoric echo is often more distinct and characteristic with whisper than with ordinary speech.

(*c*) *Metallic tinkle* is another sign of much value, and its mode of production has been the subject of much speculation and discussion. The sound is characteristic and resembles nothing else that is heard over the chest. It may occur in the course of normal respiration, or be produced only upon deep inspiration or by coughing. At other times it occurs after change of position. It is heard only over the affected portion of the chest, and it is generally associated with, but need not necessarily be accompanied by, amphoric breathing.

A number of explanations have been given to account for its formation: that it is produced by drops falling upon fluid from the inner surface of the chest, by the bursting of bubbles on the surface of fluid, or by air bubbling up through fluid from a submerged fistula. The most reasonable explanation, in view of all the facts reported, seems to be that metallic tinkle is merely a rale, or what under other conditions would be a rale, but which is modified through being produced in or near to a resonance chamber which, acting as a sounding board, gives to it its peculiar metallic quality. In a few cases the patients themselves have been able to hear the metallic tinkle, and in a case reported by Allbutt it could be heard in all parts of a large room.

Metallic tinkle may also in rare cases be heard over tuberculous cavities in the lung where the physical conditions approximate those present in pneumothorax. In 35 of this series of pneumothorax in which it was mentioned, it was present in 30 and absent in 5.

(*d*) *Succussion splash* is a positive indication of the presence of both gas and fluid in a cavity, and can be produced in no other way. Hence it is one of the most valuable signs of pneumothorax, and, having been obtained, it is only necessary to determine that it was made in the pleura, and not in in some other body cavity.

It may be readily distinguished from the succussion sound heard in pneumopericardium, as in this the phenomenon is synchronous with the heart beats, producing a peculiar churning sound resembling nothing else that is ever heard in the body. From splashing sounds produced in the stomach or colon it is to be differentiated by a careful study of its localization and by associated symptoms and physical signs. It is occasionally heard over a tuberculous cavity of large size containing considerable fluid, where the physical conditions closely resemble those of hydropneumothorax, and sometimes the differential diagnosis between these two conditions may be difficult.

The first mention of this sign is generally ascribed to Hippocrates, but Laennec was the first to clearly recognize its meaning and give a comprehensive description of its mode of production. The sound differs much in intensity in different cases, and these differences are not easy to explain; but it is a safe rule that only the co-existence of gas and fluid can be concluded from its presence, and not the quantity of either. As a rule, succussion sound

is heard without difficulty, although sometimes it is very faint, while in other cases it is so loud as to be plainly heard by bystanders. In the case of left pyopneumothorax (Plate VI) the patient plainly demonstrated the percussion splash to the entire audience occupying a large amphitheatre. Sometimes it is heard best when lying down, but in other cases it can be made out only when the patient stands or sits erect. Succussion splash is one of the most valuable indications of pneumothorax, and it is very often obtained long before the presence of fluid can be made out by percussion. It is generally perfectly safe to shake the patient vigorously enough to bring out the sign, excepting in cases in the very last stage of pulmonary tuberculosis. It is a good rule to test for succussion sound in every case of pleural disease in which the signs leave one in doubt as to the exact nature of the condition. In 54 of this series in which it was mentioned, in 41 it was present and in 13 absent.

(*e*) The *rales* heard over pneumothorax will depend upon the condition of the pleura and the lung, and do not differ from rales in other pulmonary diseases, excepting in so far as the quality of the sound is susceptible of modification by the tense pleural cavity in or near which they are produced. Therefore, the rales present in pneumothorax are not characteristic and are of no special value in diagnosis. As a rule, but few rales are to be heard, and often none, due to the fact that the pleural surfaces are not in apposition, and that the lung is retracted, inert and distant from the chest wall. Absolute stillness over a hyperresonant area with the absence of all rales is always strongly suggestive of pneumothorax.

(*f*) *Coin Sound.*—This phenomenon has been known also as the bell sound and Bruit d'Arain. It is said to have been first described by Trousseau, who made use of an ordinary pleximeter and percussion hammer. The sound is obtained by applying the ear to the front or back of the chest while another person practises instrumental percussion at a point directly opposite the listening ear. It is customary generally to use two coins, applying one firmly to the chest wall and striking it sharply with the edge of the other. In order to constitute the coin and bell sound it is necessary not only that the sound be transmitted with greater intensity through the affected side, but that it possess a clear, musical, bell-like quality which is perfectly distinctive, and whose timbre strongly suggests that of amphoric breathing.

It is uncertain whether the sound is produced by high or low tension of the contained gas, as the views of experimenters differ on this point; but it seems most likely that it is produced by the same conditions that give rise to amphoric breathing. It is a very common phenomenon in pneumothorax, and is of distinct value in diagnosis in certain cases, although, unfortunately, it is most apt to be present in pronounced cases, in which the other evidences of the condition are present and recognition therefore easy, and to be absent in the less extensive and obscure ones.

In the 25 of Emerson's cases in which it was mentioned, it was present in 20, absent in 3, and suggestive in 2. In 37 of this series in which it was mentioned, it was present in 25 and absent in 12. Such variations may be accounted for by difference in the standard adopted for the coin sound. When it is present and characteristic, it is almost although not absolutely pathogenic. Osler reported a case in which a typical coin sound was obtained over a large tuberculous cavity in the right upper lobe, and where autopsy showed the absence of pneumothorax. Such cases, however, must be infinitely rare.

**Analysis of Gas.**—When air finds its way into the pleura, it regularly goes through certain definite changes. As demonstrated by Emerson on dogs, there is an almost immediate accumulation of $CO_2$, while the oxygen diminishes. The nitrogen, meanwhile, at first remains constant, then increases relatively. The increased $CO_2$ is obtained from the neighboring tissues and from the blood. Ewald, as the result of gas analysis, concluded that the percentage of $CO_2$ was larger in purulent than in serous cases. Analysis of the gas is of no value in determining the condition of the pulmonary fistula.

Formerly it was firmly believed that the presence of air in the pleura caused inflammation of the membrane, but we now know that such inflammation, if present, is generally brought about by microörganisms that find their way to the pleura with the air. Where only sterile air enters, as in most cases of spontaneous pneumothorax, no pleuritic effusion as a rule occurs. In the 58 cases of spontaneous pneumothorax collected by Fussell and Riesman, only 1 showed hydrothorax.

The pleura possesses considerable power of absorbing gas, a power which has been extensively tested by experiment both in animals and to some extent in human beings with pneumothorax. In the main these investigations point to tolerably uniform conclusions as established, for instance, by Szupak as the result of experiments upon dogs, and comparison with cases of pneumothorax in man. He found that in the normal pleura pure $CO_2$ and pure O are absorbed at the same rate as air, while N is taken up at only one-half this rate. Air is absorbed also by the inflamed pleura, but at a less rapid rate, and, roughly speaking, the rapidity of absorption in any case is inversely as the degree of disease of the membrane.

This corresponds fairly closely with the results of clinical observations, which show that in non-infected spontaneous pneumothorax the disappearance of the gas is most rapid, while in those cases with chronic disease of the lung and pleura its absorption may be indefinitely delayed. Even in the spontaneous cases, however, no definite normal rate can be established, and according to Szupak's investigations it varies generally from twenty-six days to two months, although cases are reported widely exceeding both of these limits. It must be remembered, however, that such conclusions from clinical data are only roughly approximate, as it is not possible to determine that there has been no subsequent additional leakage of air into the pleura, nor can an accurate conclusion always be reached as to whether the pleura has remained normal or not. In general, as would be expected, recovery and disappearance of the gas are more rapid in younger, and less rapid in older and less vigorous persons.

**Course and Prognosis.**—The course of the disease will depend entirely upon the cause. In the spontaneous form where infection of the pleura is rare, the prognosis is uniformly favorable. In a few days, unless it is of the suffocative type, the patient develops a distinct tolerance to the change in the thorax. There is often comparative comfort with no complaint of dyspnœa except upon exertion, although air can still be demonstrated in the pleura. The dyspnœa, too, gradually disappears, and there is finally a return to good health, the disease having lasted for from a week to several months.

In the 58 cases studied by Fussell and Riesman there was but 1 death, and in only 1 case did effusion appear. Adams[1] has reported a case in

[1] *Boston Medical and Surgical Journal*, 1886, vol. cxv, p. 397.

which the pneumothorax lasted four years and with no exudate or other evidences of inflammation. In the traumatic cases the course and prognosis will depend upon the extent of the lesion and the question of the presence or absence of infection. The cases following thoracentesis generally do well, following the type of the spontaneous variety.

In the tuberculous cases, on the contrary, the outlook is not good. These patients generally develop a purulent exudate, and to the symptoms of the pulmonary tuberculosis are added those of secondary pyogenic infection. The fever becomes more marked and of irregular type and emaciation is more rapid. West gives the mortality as in general 70 per cent. Death may be due to the pneumothorax itself, to the subsequent empyema, or to the original disease, generally phthisis.

In a very few cases where the pulmonary disease is not very extensive and undergoes retrogression, or where infection of the pleura fails to take place, the patients recover. Moreover, in rare instances, even in pyopneumothorax in tuberculosis, recovery has followed operation for the evacuation of the pus.

Spengler[1] has reported 4 cases of pneumothorax complicating pulmonary tuberculosis, all of which went on to the cure not only of the pneumothorax, but also of the tuberculosis. He regards the prognosis in such cases as comparatively good if the exudate is serous or seropurulent and without secondary pyogenic infection. Such a favorable outcome of this complication of pulmonary phthisis, however, is not in accord with the experience of most physicians.

There is some reason for believing that with the admission of air to the pleura, and collapse or compression of the lung, a tendency to subsidence of the activity of the tuberculous process is brought about; but taking everything into consideration, the occurrence of pneumothorax in the course of any case of pulmonary phthisis can be regarded only as an accident of the greatest gravity, and as necessarily rendering the prognosis bad. The duration of life in the tuberculous form is entirely undetermined, and varies from a few hours in the suffocative cases to several years.

Hughes[2] reports the case of a young man who was living three years and two months after the occurrence of pneumothorax and in whom the condition had persisted, and who not only attended to his regular business, but was in the habit of shaking himself in order to amuse his friends by the succussion sound.

**Varieties.—Closed Pneumothorax.**—By this is meant a pneumothorax in which the fistula in the lung or in the chest wall has become closed so that there is no longer any communication between the pleural cavity and the atmosphere. Such closure may be brought about either by the sealing of the orifice by inflammatory exudate or by the valve-like action of the tissues. The lung in its collapse tends naturally to close over any small lesion, so that cases caused by small wounds of comparatively healthy lung tissue tend soon to become of this closed variety. Cure of any case of pneumothorax can take place only through such closure of the fistula.

In this type, favorable progress and likelihood of permanent cure are directly proportionate to the soundness of the lung and pleura. It is especially necessary in such cases that any overexertion should be avoided

[1] *Ztschft. f. Tuberc. u. Heilst.*, 1901, Band ii.
[2] *Guy's Hospital Report*, 2d series, vol. viii.

that might re-open the fistula, and so perpetuate the condition. This variety is the regular type in the spontaneous form, and in that due to thoracentesis, while it occasionally occurs in phthisis, especially when the pulmonary lesion is not advanced and extensive.

**Open Pneumothorax.**—Open pneumothorax is that variety in which air passes more or less freely both into and out of the pleura, and it remains of this type until closure of the fistula takes place. Here belong those cases of advanced phthisis in which a fistula of considerable size occurs in the lung, generally a ragged hole opening into a cavity and in which the tendency to repair is absent or slight on account of the characteristic disposition of the circulation in tuberculous tissue. The majority of the cases of empyema in which the pus has perforated into a bronchus and is expectorated, as well as those in which a free external opening has been made in the chest wall, are also included.

Open pneumothorax usually becomes infected, and as the inflammatory process advances the difficulties in the way of ultimate closure of the fistula become greater, although the cavity may gradually become smaller and ultimately be obliterated. This unfavorable view does not apply to the operative cases, chiefly of empyema, where, in the presence of healthy lung, the natural tendency is toward healing.

Open pyopneumothorax of the internal variety is to be recognized by the periodical expectoration of pus when the cavity empties itself, as well as by the physical signs which, while not positively diagnostic, are often suggestive.

**Valvular or Suffocative Pneumothorax.**—By this is meant that form of the disease in which, owing to a valve-like action of the fistula, air is freely admitted into the pleura, but escapes less readily from it. The chest now acts like a pump, and, as was first demonstrated by Bouveret, the violent expiratory efforts raise the pressure in the pleura until the thorax is over-distended, the mediastinum and its contained viscera suffering extreme displacement. The patient shows marked dyspnœa, which steadily becomes more urgent, and may result fatally unless relieved.

**Pneumothorax Acutissimus.**—This term is applied to the cases with death resulting within a few hours of the onset. This may be because the patient was already ill with antecedent tuberculosis, or because there is a valvular fistula with very high positive pressure rapidly developed and unrelieved. It is sometimes also called suffocative pneumothorax, and is not clearly distinguished from the preceding group.

**Artificial Pneumothorax.**—It was proposed by Murphy[1] to treat certain cases of pulmonary tuberculosis by bringing about collapse of the lung through the production of pneumothorax artificially by the introduction of sterile air or nitrogen. This treatment was based upon the observation that there is a tendency for the tuberculous process to become quiescent in lungs compressed by fluid or collapsed by reason of pneumothorax.

Murphy's method is as follows: An ordinary aspirating needle is sterilized and attached by a sterile rubber tube to a glass vessel containing sterile absorbent cotton, through which the gas is to be filtered. This, in turn, is attached to a small gasometer, by means of which the amount of gas injected can be measured and the pressure regulated. The chest wall having been prepared, the needle is forced just through the parietal pleura, and the patient directed to take a long breath, which generally starts the flow. From 50 to

[1] *Journal of the American Medical Association*, July 23, 1898.

200 cubic inches of gas are introduced, or until the lung has collapsed and no breathing sounds can be heard over it.

The needle is then withdrawn, and a firm pad placed over the puncture to prevent subcutaneous emphysema, an accident which fairly often happens. The patients complain of some pain and dyspnœa, but generally soon become used to the changed condition. This method was practised for several years, but has now been generally abandoned.

**Double Pneumothorax.**—This has been reported in a few cases, but is extremely rare. Under these circumstances life can be maintained at all only if some lung tissue remains distended, and if the fistulous opening is small enough to allow some inflation of the lungs on inspiration. These cases always die within a few hours of the onset.

**Subphrenic Pyopneumothorax (Pyopneumothorax Subphrenicus).**—This term has been applied by Leyden to a rare condition in which a subphrenic abscess contains air or other gas. Such a condition may be produced by perforation of any hollow abdominal viscus, with the formation of an abscess immediately beneath the diaphragm. Cases have arisen from the perforation of the vermiform appendix, stomach, duodenum, and gall-bladder, and from hepatic and splenic abscess, but the most common cause is ulcer of the stomach or duodenum. The abscess containing gas, as well as pus, lies between the liver and the diaphragm, and is limited laterally by the falciform ligament. As it may be situated either on the left or right of this structure, it may simulate disease of either the left or right pleura, and the resemblance may be very close.

The diaphragm may be displaced upward as high as the third rib, the mediastinum being crowded toward the opposite side and the heart correspondingly moved. The liver is also pushed downward and the other abdominal viscera may be displaced. Over the lower portion of the chest, corresponding to the abscess cavity, there may be tympanitic resonance, taking the place of liver or splenic dulness. The respiratory murmur may be diminished or suppressed, also the vocal fremitus, and there may be metallic tinkle, succussion splash, and the coin sound. Thus the signs may be the same as those of pyopneumothorax. It is of interest in this connection chiefly on account of the extreme difficulty with which it can be distinguished from true pneumothorax.

The differentiation will generally depend upon the history of antecedent disease of the abdominal organs, the absence of cough and dyspnœa or cyanosis, together with the absence of distention of the chest or bulging of the intercostal space, and the presence of normal respiratory murmur over the greater part of the chest. In some cases amphoric breathing is heard at the very bottom of the chest immediately above the abscess.

**Diagnosis.**—Well-marked cases can generally be recognized at a glance. The sudden pain and overwhelming dyspnœa and cyanosis, the distended thorax, with the displacement of the heart, and the other characteristic signs make the nature of the trouble obvious. In other cases the diagnosis is one of the most difficult, especially when the lesion is one of limited extent, and where the symptoms are mild; probably under these circumstances a good many cases are overlooked. Among the best single clues to the nature of the trouble are very marked displacement of the heart, with amphoric breathing, or absence of respiratory sounds over a resonant area of the chest. Among other signs of value are movable dulness and hyperresonance extending beyond the ordinary limits of normal resonance.

The other conditions from which it may be difficult to differentiate pneumothorax are:

(*a*) *A Large Tuberculous Cavity.*—At times this diagnosis may be extremely difficult, but in the case of the cavity, displacement of the heart and of the liver are absent, or the heart may even be drawn toward the cavity if the disease is of long standing; the chest is less fixed, and the intercostal grooves are not lost. Also, the amphoric phenomena are generally less striking and are heard over a smaller area than in pneumothorax. Shifting dulness with change of position is not present; also, over a cavity pectoriloquy is apt to be present; moreover, the signs are generally at an apex which should always make one suspicious of a diagnosis of pneumothorax. In the case of a cavity, the symptoms are apt to be of gradual onset without the sudden attack of pain in the side, dyspnœa, and distress that so often usher in the pneumothorax.

(*b*) *Pleurisy with Effusion* with amphoric phenomena over the apex of the lung. In this these signs are limited to the apex, while there is evidence of a large amount of fluid in the lower part of the chest. Succussion splashes and metallic tinkle are absent. Occasionally the use of the needle may be necessary to settle the question of the presence or absence of air.

(*c*) *Pneumonia.*—Occasionally pneumonia of the upper lobe, most often the right, and especially at the beginning of resolution, may give a marked tympanitic percussion note with distinct metallic quality, together with cavernous breathing; but the absence of metallic tinkle and succussion splash, with the persistence of vocal fremitus and the absence of true amphoric breathing, together with the history of pneumonia and the absence of ordinary symptoms of perforation of the lung, will usually make the diagnosis clear.

(*d*) *Diaphragmatic Hernia* is a rare condition which it may be impossible to differentiate from pneumothorax during life. The special characteristics of subphrenic pneumothorax have already been given.

The diagnosis of the special type of pneumothorax may also offer difficulties.

Spontaneous pneumothorax can be assumed only when the history, the physical signs, the general behavior of the case, and the absence of tubercle bacilli in the sputum all indicate the absence of tuberculosis; but it is probable that a fair number of the so-called spontaneous or idiopathic cases are nevertheless the result of a slight undiscoverable tuberculous lesion.

The valvular form is to be recognized by the extreme distention and immobility of the chest, the overwhelming dyspnœa, relieved by the insertion of a cannula, together with the rapid return to positive pressure on removing the cannula. Wintrich claimed that the change of pitch of the percussion note on opening the mouth indicated an open fistula, but it is doubtful if we have any signs which enable us to differentiate positively between closed and open non-valvular pneumothorax.

**X-rays.**—On examination with the fluoroscope the displacement of the heart shadow to the opposite side can be clearly made out and its pulsation can often be seen in the new location.

Examination of the affected side of the chest in a case of hydropneumothorax or pyopneumothorax, with complete collapse of the lung and with the patient in a sitting posture, shows an abnormally light, transparent area above the level of the fluid as compared with the opposite side. This corresponds to the empty thoracic space. At the bottom of the chest the fluid shows as an opaque area with a perfectly horizontal surface, the upper

border of which remains horizontal, shifting with any change in the position of the patient, and wavy motion of the surface can often be seen on shaking the patient, and at times waves synchronous with the heart beats can be made out.

The retracted lung may be seen as a shadow applied against that of the mediastinum, a shadow which is said to be more dense if the lung is markedly tuberculous. The level of the fluid is seen to rise with inspiration and fall with expiration, a phenomenon which has already been explained as the result of the reversing of the vault of the diaphragm. When the patient is examined lying on his back, the diseased side shows a general shadow throughout, because the fluid has distributed itself evenly over the posterior thoracic wall, and hence gives a fluoroscopic picture that cannot be distinguished in this position from that of pleurisy with extensive effusion. In the sitting posture the picture in hydropneumothorax is characteristic and may materially help to a diagnosis.

Fewer cases would pass unrecognized if the frequency of the disease were more widely understood, and if a thorough search for all the signs of pneumothorax were more often made in all cases of pulmonary or pleural disease in which the nature of the malady is at all obscure. It should be remembered that the only distinctive single sign of pneumothorax is the succussion sound, which may be regarded as almost pathognomonic, provided it can be determined that it is not produced in one of the abdominal hollow viscera.

**Treatment.**—Prophylaxis is of avail only against the small group of cases following thoracentesis. The points to be borne in mind are: to avoid using a larger needle than is necessary; to employ only moderate suction; to remove the needle at once upon the occurrence of pain, dyspnœa, or persistent coughing; and to remove at each operation only a moderate amount of fluid, generally not more than one liter.

In any given case of pulmonary tuberculosis the likelihood of the occurrence of pneumothorax is so slight that it is doubtful if it is wise to restrict the activities of the patient with this in view.

When spontaneous pneumothorax occurs, unless it be of the suffocative type—a rare occurrence, no active treatment is generally called for. The patient should for a considerable period avoid such overexertion or deep breathing as might tend to re-open the recently closed fistula in the lung, and should be kept absolutely quiet and in bed until it can be assumed that the aperture is closed.

In urgent cases of pneumothorax energetic treatment is required. In the suffocative type, relief of the suffering is to be sought by the insertion of a cannula in the chest to relieve positive air pressure, and the gas can often be heard as it rushes from the tube. The cannula may either be left in place or be re-inserted as needed, when pressure rises and the symptoms return. Forcible aspiration of air should not be attempted lest the process of closure of the fistula be interfered with. Occasionally it is necessary to make a free opening in the chest wall, thus converting the case from a valvular to an open pneumothorax.

Morphine may be needed at the outset, as well as free stimulation of the heart by alcohol, or by camphor or other rapidly diffusible stimulants administered hypodermically.

Strapping of the affected side has been recommended, and occasionally gives some relief, but as often fails. When for any reason the chest is punctured in pneumothorax, the utmost care must be exercised lest the pleura

become infected, and the site should be well cleansed and prepared as for thoracentesis, while, by the use of gauze over the tube, the possibility of the admission of unfiltered air into the pleura can be guarded against. Traumatic cases, as a rule, require no further medical treatment.

In hæmo- and hydropneumothorax the fluid should in every case be left undisturbed for a considerable period until closure of the fistula has taken place. Where the effusion is moderate in amount it can be neglected; where extensive, it may later be withdrawn, but only with great caution and in small amounts. Where it accumulates rapidly and in large quantity it may be necessary to relieve it at once.

In pyopneumothorax, especially when complicating pulmonary tuberculosis, widely divergent views are held regarding the best subsequent procedure. It is advised by some to open the chest freely as soon as the presence of pus can be proven; it is equally strongly urged by others to avoid operation in such cases, and to administer only general medical treatment.

It is a situation, however, for which no general rule can be formulated to apply in all cases. When the symptoms of septicæmia are pronounced or when the pus is rapidly accumulating and dyspnœa is increasing, the dangers and discomforts from these conditions are greater than those inseparable from a free opening of such a chest, and the treatment should be the same as for empyema, that is by free incision, or the removal of portions of one or more ribs.

On the contrary, when, as not infrequently happens, these symptoms are not threatening, when the patient becomes adjusted to the condition, and when he exhibits little more than the symptoms of the preëxisting tuberculous disease, it is wiser to avoid opening the thorax. In such circumstances as these, many patients continue for months or even several years in comparative comfort. In each patient the decision must be arrived at through balancing the dangers and discomforts produced by the operation against such relief of the symptoms as can fairly be promised from it.

Spengler recommends the repeated withdrawal of 500 to 700 cc. of fluid at intervals of one to four weeks, and reports four cases cured in this way.

Various devices have been suggested to prevent collapse of the lung and the development of pneumothorax when for any reason the thorax has to be opened.

Sauerbruch[1] experimented with and recommended a cabinet which surrounded the chest, the head and abdomen being outside. The air was partially exhausted from this chamber and thus a lower pressure was maintained about the chest than existed within the lung, and so collapse of the latter was impossible. Brauer[2] accomplished the same result by a mask or box into which the head was placed and fitted with an air-tight collar for the neck. Air pressure was thus raised above the normal in the case, and the same result accomplished as by Sauerbruch's more extensive device. These are interesting mechanical devices and theoretically correct, but hardly practicable therapeutic appliances.

Where an abdominal viscus has perforated into the pleura, the indications are for immediate operation. Those very rare cases in which the gas in the pleura is the result of the exudate in empyema are of course to be regarded as empyemata, and to be so treated by operation without delay.

[1] *Mitth. a. d. Grenzgbt d. Med. u. Chir.*, 1904, Band xiii, p. 399.
[2] *Ibid.*, p. 482.

# CHAPTER XXII.

## DISEASES OF THE MEDIASTINUM.

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**Introduction.**—The mediastinum is that portion of the thorax bounded by the pleuræ on each side, the sternum in front, and the vertebral column behind. It extends from the root of the neck to the diaphragm and contains the heart with its efferent and afferent vessels, the œsophagus, the trachea and primary bronchi, the thymus gland; the vagus, phrenic, and sympathetic nerves; the thoracic duct, lymph nodes, lymph vessels, and loose areolar tissue. The mediastinum is variously subdivided by anatomists into anterior and posterior; anterior, middle, and posterior; superior and inferior, with further division of each into anterior, middle, and posterior. The heart and trachea constitute the plane of division between anterior and posterior in the first classification: the middle mediastinum contains the heart, trachea, primary bronchi, ascending aorta, pulmonary vein, and vena cava superior, while the structures in front and behind these occupy respectively the anterior or posterior mediastinum: in the last classification the upper border of the heart divides the space into superior and inferior mediastinum.

As ordinarily used, the term *diseases of the mediastinum* is purely a conventional one. It does not comprise all diseased conditions of the organs situated in the mediastinum, but only such as are not conveniently grouped under other headings. Under diseases of the mediastinum it is convenient to consider neoplastic and inflammatory conditions which originate in or chiefly affect the mediastinum. The diseases of the trachea, bronchi, œsophagus, thymus, heart, and great vessels are described elsewhere, and these structures will be considered here only in so far as they are affected by tumors and inflammations of the general mediastinal space. Almost all of the conditions to be described have their main seat in the superior mediastinum; it may be convenient at times to further divide this into an anterior and a posterior part by a plane passing laterally through the trachea, but a strict anatomical subdivision will not add to the clearness of the subject. Rather it is the purpose to consider the mediastinum as a whole and to discuss the effect of diseased conditions on its contents, with only occasional reference to an anterior and a posterior, a superior and an inferior mediastinum.

### TUMORS OF THE MEDIASTINUM.

Of diseases of the mediastinum tumors form the group of greatest interest and importance. Both primary and secondary tumors occur in the mediastinum. Primary tumors may take their origin from any of the structures

in this region. Probably their most frequent origin is in the mediastinal lymph nodes and thymus. Secondary tumors enter the mediastinum either by metastasis or by direct extension. Unfortunately in most cases it is not possible to determine definitely the point of origin of a tumor in the mediastinum; hence it is not practicable to discuss them with reference to their place of origin. A structural classification would be rational and is highly desirable, particularly with regard to prognosis. The difficulty is that clinically it is so often impossible to diagnosticate accurately the character of tumor present; nevertheless a structural classification will be followed and the various forms of tumor considered separately as far as is feasible.

## Primary Tumors.

In the mediastinum with its complex content a variety of primary tumors may develop. Fibroma, lipoma, chondroma, osteochondroma, myoma, sarcoma, carcinoma, simple cyst, dermoid cyst, and teratoma occur. All of these except sarcoma, carcinoma, and rarely teratoma, are benign, in the sense that they do not invade or metastasize. However, since the mediastinum is a confined space of small dimensions, containing many important structures, any one of these tumors in its growth may produce serious pressure symptoms, and tumors, which in other parts of the body are of little moment, here may prove fatal, even before the tumor has attained any very great size.

**Fibroma.**—Fibroma is exceedingly rare in the mediastinum. Hare[1] was able to collect only 7 cases and some of these are undoubtedly incorrectly included in this group. Hoffmann[2] points this out and accepts 5 cases from the literature, but of some of these the original report was not accessible to him. The case of Barclay[3] included by Hoffmann may be objected to on the following grounds: the duration of symptoms was only ten weeks, while the tumor was larger than a cocoanut, compressing the trachea and moulded over a part of the pericardium; on the peritoneum were minute nodules like millet seed, stated by the author to be of the same nature as the large tumor. From this description it would seem that the tumor should be classed as fibrosarcoma rather than fibroma. To the case of Pastau[4] similar objection can be made, for in the left lung were fairly numerous fibrous tumors scarcely to be regarded, in the light of present knowledge, as other than metastases from the mediastinal tumor. Further, the description of the mediastinal tumor itself suggests the invasive growth of a slowly developing malignant tumor (fibrosarcoma) rather than the expansible growth of a benign one (fibroma). Roberts[5] speaks of a case of Steven which the former considered malignant fibrosis associated with pronounced rheumatic manifestations. Descriptions of the cases of Oberstimpfer and MacDonald, detailed enough for criticism, were not available, and no recent cases were found. Even if the term fibroma is extended so as to include these slowly growing fibrosarcomata of the mediastinum, the condition still is very rare.

[1] *The Pathology, Clinical History, and Diagnosis of Affections of the Mediastinum*, Philadelphia, 1889.
[2] Nothnagel's *Spec. Path. und Therapie*, 1897, viii.
[3] *Lancet*, 1864, xli, 244.
[4] *Arch. f. path. Anat.*, etc., 1865, xxxiv, 236.
[5] Allbutt's *System of Medicine*, 1899, vii, 100.

**Lipoma.**—Lipoma is also rare in the mediastinum. Seven cases have been collected. Three of these (the cases of Cruveilhier,[1] Morel-Lavallée[2] and Krönlein,[3] the latter operated on by Langenbeck and sometimes referred to under his name, also reported by Vogt[4]) showed a subcutaneous lipoma which had grown from or at least was continuous with a lipoma situated in the anterior mediastinum. At autopsy in Krönlein's case there was a rounded lipoma as large as a child's head completely filling the anterior mediastinum. In the case reported by Fitz[5] no extrathoracic tumor was present, but a lipoma about the size of a new-born child's head lay to the left of the pericardial sac, connected by a pedicle to the fat tissue of the anterior mediastinum. In this case the tumor evidently developed at an early period of life, for the lower lobe of the left lung was hypoplastic, not compressed. Still the patient lived to adult life without symptoms from the tumor, and death at thirty-four resulted from a purulent pericarditis. In this case an exploratory puncture through the sixth left interspace in the axillary line yielded a bit of soft tissue which proved to be fat tissue.

Ewing[6] found in the dissecting room a large mediastinal lipoma in a fat, middle-aged male subject. The tumor was lobulated and "sprang by a pedicle about 10 cm. broad from the tissue of the anterior mediastinum. The pedicle ramified from this point in many directions, involving the parietal pericardium, passing up along the bronchi, trachea, and great vessels, partly surrounding the descending aorta and infiltrating the diaphragm. The main mass of the tumor consisted of five distinct lobules of fat tissue, each about the size of a goose-egg, loosely attached to one another by broad pedicles. These were packed together in the lower part of the left pleural cavity, occupying rather more than one-half of this space." Fothergill and Jurint (cases cited by Hare) have each reported a case.

**Chondroma.**—Chondroma and osteochondroma are very infrequent. Tumors of this group could possibly arise in the mediastinum from the under surface of the sternum and costal cartilages, from the anterior surface of the vertebral column, or from bits of cartilage developmentally displaced from bronchi or trachea. Wiesmüller[7] reports a case where a chondroma grew from the sternum and increased rapidly in size so as to produce a bulging of the skin as well as pressing into the anterior mediastinum.

**Myoma.**—Myoma may arise from the wall of the œsophagus, trachea, or bronchi. Myoma arising from the œsophageal wall is not excessively rare, but the tumors are small, closely attached to the œsophagus, and rarely give symptoms unless the œsophagus is obstructed. In one case (Coats)[8] the myoma was pedunculated and lay within the lumen of the œsophagus. In a recent case at the Long Island Hospital, Boston, and in one reported by Eberth, the tumors, though lying outside the wall of the œsophagus, were practically situated below the bounds of the mediastinum. These three cases scarcely belong to the present consideration. In a case at the Boston Insane Hospital there were symptoms of œsophageal obstruction six months before

[1] *Traité d'anat. path. gén.*, 1856, iii, 315.
[2] Cited by Cruveilhier, *loc. cit.*, 322.
[3] *Arch. f. klin. Chir.*, 1877, xxi, supplement 157.
[4] *Inaug. Diss.*, Berlin, 1876.
[5] *American Journal of the Medical Sciences*, 1905, cxxx, 785.
[6] *Transactions of the Association of American Physicians*, 1905, xx, 66.
[7] *Ref. Cent. f. allg. Path. u. path. Anat.*, 1905, xvi, 620.
[8] *Glasgow Medical Journal*, 1872, iv, 201.

death, and at autopsy there was a myoma, 3.2 x 3 x 2.5 cm., lying without the wall of the œsophagus, but obstructing its lumen through pressure. In the cases of Fagge,[1] Illig,[2] and Pichler[3] there were tumors of moderate size in association with the œsophagus, but no symptoms or physical signs of them during life. Details of several other reported cases are not available.

Simple benign tumors, as we have seen, are of infrequent occurrence in the mediastinum. Most often they are accidental postmortem findings. Cases which, during life, have shown symptoms due to their presence, are as yet too few to justify any attempt to construct a special symptomatology. It is sufficient to bear them in mind in connection with patients showing slight long-continued signs of mediastinal tumor. If diagnosed there is a good chance of successful surgical removal.

In contrast to the tumors already discussed are those remaining for consideration (sarcoma, carcinoma, cyst, and teratoma). These are not excessively rare, but form a fairly definite though small proportion of hospital medical cases (1 in 500 at St. Bartholomew's Hospital, London). Furthermore their clinical course and physical signs are sufficiently characteristic to lead to a correct diagnosis in the larger percentage of the cases. Consequently a knowledge of them is of considerable importance.

**Sarcoma.**—Sarcoma, of all tumors of the mediastinum, is of most frequent occurrence, although in the older books carcinoma is given as the most common primary tumor. This, however, is undoubtedly due to errors in terminology and diagnosis. Hare, in whose collection of 520 cases of mediastinal disease 98 are given as sarcoma and 134 as cancer, merely classifies them according to the author's diagnosis, without any criticism of its correctness, and does not exclude secondary tumors. This apparent frequency of cancer is due to the earlier use of this word for any cellular malignant tumor. This is shown by the fact that the larger part of Hare's cases of cancer antedate 1880, while the reverse is true of the sarcomas. Hoffmann recognizes the insufficiency of evidence for many of the cases of cancer and points out the necessity of careful microscopic study before diagnosis. The very great preponderance of sarcoma over carcinoma in the recent literature shows the comparative infrequency of the latter. At present, classifying tumors on a structural basis, we reserve the terms carcinoma and cancer for tumors clearly epithelial in structure and cell grouping. Such are undoubtedly infrequent in the mediastinum, while tumors structurally of the sarcoma group are relatively frequent.

Sarcoma can originate in the loose connective tissue of the mediastinum, in the peribronchial and mediastinal lymph nodes, and in the thymus. It is not possible to determine which of these is the most common point of origin for these tumors, since in few cases at autopsy are the relations such as to definitely reveal the beginning point of the tumor. The presence in some of the tumors of bodies of the structure of the concentric corpuscles of Hassall serves as evidence of a thymic origin and is the probable reason for the belief that the thymus or its remains is the common source of sarcomas of the mediastinum. However these are not very frequently found and when present may mean no more than that the tumor has included in its growth remains of the thymus, though starting elsewhere.

[1] *Transactions of the Pathological Society of London*, 1875, xxvi, 94.
[2] *Inaug. Diss.*, Giessen, 1894.
[3] *Prag. med. Woch.*, 1897, xxii, 455.

Structurally we may divide most sarcomas of the mediastinum in two classes, spindle-cell sarcoma and lymphosarcoma. A very few are giant-cell sarcoma or chondrosarcoma. Of these lymphosarcoma is the more common. Tumors of both kinds vary considerably in size, in consistence, and in color. At autopsy they are usually found to fill completely the mediastinal space and compress various of the midthoracic structures. It is unusual for mediastinal sarcomas to show any very great amount of invasive growth and they compress rather than destroy. Generally the tumor is of moderately firm consistence, gray to yellowish-gray or pinkish-gray in color, often mottled with red areas of hemorrhage or grayish-yellow foci of necrosis. The consistence depends on the amount of intercellular substance present and shows marked variations. In general the more rapidly growing tumors are softer. Tumors of the spindle cell group are apt to be of a homogeneous texture and regular contour, while the lymphosarcomas tend to be lobulated and consist of tumor masses more or less separated by bands of connective tissue.

Histologically the spindle-cell sarcomas are composed of closely packed cells of a general spindle shape and varying size, rarely very large. Adjacent cells usually have their long axes parallel and such cell groups surround a bloodvessel. The cells have a single elongated nucleus of moderate size and fairly rich chromatin content. These cells belong to the connective-tissue group and form both fibroglia[1] and connective-tissue fibrils. The amount of intercellular substance thus formed varies greatly in amount in different tumors. The vascular supply is relatively rich in most cases and the bloodvessels are thin walled, especially in the rapidly growing cellular tumors. The spindle-cell sarcomas form a group of tumors the extremes of which are represented on one side by the so-called fibrosarcomas, on the other by very cellular tumors composed of irregular cells approaching a round shape. The former grow slowly, the latter rapidly. The majority of reported cases are of the intermediate type.

Lymphosarcomas are made up of round cells lying in a reticulum. The cells in different cases may vary in size, but are usually small and all represent stages in the lymphocyte group of cells. The cells lie in a meshwork of fibrils (reticulum). Applied to the fibrils are a varying number of larger cells with clear protoplasm and vesicular nucleus (cells of the endothelial type). The latter cells are often phagocytic for other cells. Frequently they are multinucleated (small giant cells). The tumors are moderately vascular. The characteristic part of these tumors is the small round cell of the lymphocyte type which has a deeply staining nucleus and relatively little cytoplasm. In well-preserved specimens the nuclei show rather coarse chromatin masses tending to a peripheral grouping. The reticulum may be scanty or abundant and the number of cells of the endothelial type varies greatly. Some of these tumors grow slowly, others rapidly. Metastasis when it occurs is more commonly into lymph nodes first, later into lungs or abdominal viscera.

Under the term lymphosarcoma we include a group of tumors of a general type, with extremes of cells and intercellular substance, as in the spindle-cell series. To them a variety of names have been given, lymphoma, malignant lymphoma, lymphocytoma, round-cell sarcoma, lym-

[1] Mallory, *Journal of Medical Research*, 1903, x, 334.

phadenoma, etc., and the attempt has been made to distinguish different varieties, as lymphoma (benign) and lymphosarcoma (malignant). This has led to confusion in the clinical consideration. It seems more correct and in every way preferable to group all of the tumors together under one term, and for this we have selected lymphosarcoma as having the advantage of usage and fairly well expressing the nature of the tumor.[1]

In this group are not included the enlarged lymph nodes of leukæmia and Hodgkin's disease. These are systemic diseases in which the mediastinal lymph nodes may be affected; if they are tumors those in the mediastinum are in most cases clearly of the nature of metastases. Cases, however, in which there is a tumor of the mediastinum having the histological characteristics as described by Reed, Longcope, and others for Hodgkin's disease, but no general lymph-node involvement, may be included in the lymphosarcoma group for the present.

**Age.**—In 100 collected cases of sarcoma of the mediastinum the age is divided between the decades as follows:

| | | | | | |
|---|---|---|---|---|---|
| Between | 1 | and | 10 | years | 9 cases. |
| " | 11 | " | 20 | " | 20 " |
| " | 21 | " | 30 | " | 17 " |
| " | 31 | " | 40 | " | 18 " |
| " | 41 | " | 50 | " | 19 " |
| " | 51 | " | 60 | " | 12 " |
| " | 61 | " | 70 | " | 4 " |
| " | 71 | " | 80 | " | 1 " |

Sarcoma is not uncommon in the first decade and has been reported soon after birth. In the decades between ten and sixty the regularity of distribution is very noticeable. There seems to be no age at which sarcoma of the mediastinum is particularly common and none at which it may not occur. It is somewhat more common in males; in these cases two-thirds were male, one-third female.

**Symptoms.**—The character of the symptoms in sarcoma of the mediastinum varies much in individual cases. However two general types occur: cases of gradual onset and progressive development of symptoms; cases with sudden appearances of symptoms and a rapid subsequent course. The former type is the more usual.

Ordinarily the patients give a history of an increasing shortness of breath, particularly following moderate exertion; or there is a persistent cough. Very frequently both are present, and combined with them is a sense of fulness, with feeling of oppression in the chest, with or without moderate

[1] Much confusion exists in regard to tumors of this group and their relation to myeloma, leukæmia, and Hodgkin's disease. That there is a very close relation is believed by many and there is much evidence favoring this. It is with some hesitancy that the writer has retained the term lymphosarcoma because it suggests a close relation to the sarcoma group. The two he considers histogenetically distinct and prefer the name lymphocytoma as suggested by Ribbert for the lymphocyte group. However, it is difficult to change established terms, and so the name lymphosarcoma is retained with this protest.

While there is undoubtedly a close relation between these localized tumors and some of the generalized processes, there is enough difference in their clinical aspects to warrant separation, until more exact knowledge is gained from careful cytological study of many cases, from which material has been preserved by methods adapting it to the application of the newer staining processes. This promises to yield a better basis for classification.

pain. Such symptoms gradually increase in severity, and within a few months are severe enough to cause the patient to consult a physician either for dyspnœa or for the discomfort or pain in the chest.

With the other group of cases there are, as it were, no premonitory symptoms. Quite suddenly dyspnœa develops or there may be an attack of suffocation. Sometimes it is a severe cough or pain in the chest which warns the patient of impending danger. These cases may become quiescent and remain so for some length of time, but this is not apt to be the case, since the average duration of sarcoma in this region is less than one year.

There are many variations from these types. Symptoms are almost entirely the result of pressure; what they are depends on the structures pressed upon and the degree of the pressure. Here a tumor, while still small, encroaches on some important mediastinal structure with resultant early definite symptoms; there another, differently situated, grows to considerable size before any structure is functionally involved, and symptoms appear tardily.

The most common symptom is dyspnœa. Rarely is this absent; ordinarily it is an early symptom and almost every patient at some time during its course is dyspnœic. Frequently dyspnœa is the most troublesome symptom. It may be the result of pressure on the heart or lungs, obstruction of the trachea or bronchi, chronic passive congestion of the lungs, or irritation or destruction of the recurrent laryngeal nerve, and these causes may act singly or in combination.

The dyspnœa in most cases occurs in the form of recurrent attacks, at first only after physical exertion or emotion. Gradually the attacks become more and more frequent and less dependent on exciting causes. Finally they become practically continuous. In the later stages the patient is prevented from assuming a recumbent posture and sleep is more and more interfered with. In not a few cases death results from suffocation, and in almost all dyspnœa has largely contributed to the lethal outcome.

Pain is a frequent symptom, particularly in the later stages of the disease. Often this is severe, but in most cases it is not excessive. At first there is usually only a sense of weight and oppression in the chest; later, more definite pain. Not infrequently moderate paroxysms of pain occur which radiate up the neck or down the arm. There may be localized numbness or pain in one arm, the result of pressure on the brachial plexus or its roots. More rarely one sees intercostal pain due to pressure on the intercostal nerve roots near their exit from the spinal column. A number of cases have run an almost painless course and that constant intense boring pain which characterizes many aneurisms is quite exceptional.

Patients with sarcoma of the mediastinum generally cough. This cough may result from vagus irritation. More commonly it is the result of bronchitis associated with pressure on the respiratory tract. In some cases cough is a dominant feature, persistent and difficult to control. Often there are paroxysms of cough separated by varying periods of freedom. In a number of cases cough has been slight or even absent. With the cough there is practically always a mucous or muco-purulent expectoration, often very copious. Frequently the sputum is blood streaked and in a few cases there is hæmoptysis suggestive of pulmonary tuberculosis. Examination of the sputum yields no positive diagnostic evidence.

Dysphagia occurs in some cases, but is not very common. The œsopha-

gus, by its position and structure, is quite well guarded from pressure obstruction arising from mediastinal neoplasms.

Hoarseness and a weak voice are common later symptoms and there may be aphonia. These result from pressure on the recurrent laryngeal nerves; but it should be borne in mind that paralyses of the vocal muscles may be present without change of voice and remain undetected unless the throat is examined with the laryngoscope.

With the above-described symptoms there is a loss of appetite, progressive muscular weakness, and a decrease of subcutaneous fat, all signs of a serious progressing malady. In sarcoma the course of the disease is, in most cases, relatively a rapid one. Usually death ensues in about six months after the development of definite symptoms and not very many live longer than one year. Slowly growing, more fibrous tumors extend over a longer period, but they are not the more common form. On the other hand, the course may be fulminant, as the one reported by Jaccoud[1] with death in eight days after the first symptom.

**Physical Examination.**—Inspection probably yields most diagnostic information. A deformity of the upper anterior thorax, consisting of a median or medio-lateral bulging of the chest wall may be evident at a glance. In other cases no deformity of the bony wall of the thorax exists, but a slight fulness of the intercostal spaces adjacent to the sternum may be noted. Accompanying a prominence of the chest wall, or independent of deformity, a localized pulsation may be seen. This is much more characteristic of aneurism, but may occur in mediastinal tumor, either as a transmitted aortic pulsation, the pulsation of a distended vein, or the pulsation of an extremely vascular tumor. The latter may be even expansile in character and closely simulate an aneurismal pulsation; however, a systolic bruit heard over such an area is extraordinarily rare in tumor, while common in aneurism.

In a large percentage, particularly in the later stages, a dilatation of the superficial veins of the thorax and neck is apparent, and this is more apt to be unilateral than bilateral. Not infrequently the jugular veins stand out as prominent cords, or tortuous veins of considerable diameter may be seen coursing over the anterior chest; corresponding perhaps in situation to normal vessels, although very far exceeding the normal in size. Sometimes these vessels are limited in distribution to the chest wall in front, between the clavicle and third or fourth ribs. In other cases they may extend down to or even below the level of the attachment of the diaphragm, appear in the back, and extend up along the neck on to the face. With involvement of the veins of the neck and face exophthalmos may be produced. Similarly the veins of the arm may be distended and tortuous.

Localized cyanosis of the skin is not uncommon accompanying the venous dilatation and corresponding to the distribution of the dilated veins, although it may occur without venous dilatation. In other cases cyanosis is more general, being due to interference with normal respiration or the result of defective cardiac action. In the latter cases the cyanosis is of the nature of the cyanosis common in cardiac and respiratory diseases.

Rather more striking than cyanosis is localized subcutaneous œdema, with or without prominent superficial veins. The distribution of this varies in individual cases as does that of the dilated veins. Localized

[1] Cited by Riegel, *Arch. f. path. Anat.*, etc., 1870, xlix, 212.

venous dilatation, cyanosis, and œdema result from pressure on veins, more commonly pressure on the superior vena cava or some of its larger branches. As the obstruction increases, collateral circulation takes place by way of the internal mammary, the intercostal, and the azygos veins. In some cases this collateral circulation is sufficient to prevent signs of venous obstruction. The superior vena cava is rarely obstructed near enough to the heart to occlude the azygos vein. In that case the collateral circulation is mainly by way of the internal mammary and superficial epigastric veins.

In a number of cases a tumor will be visible in the neck, either in the sternal notch or above the sterno-clavicular articulation. Careful inspection of the neck may reveal deviation of the trachea from the midline or the trachea is seen to ascend a trifle obliquely from the sternal notch, both indicative of an intrathoracic mass pressing the trachea to one side.

In a few cases the position of the patient is characteristic. Some assume an attitude with the head bent forward and chin resting on the sternum. In one patient a decubitus of the forehead was produced from pressure on a table as the patient sat bent over. In other cases greatest comfort is found with the head thrown back. Some can lie only on one side. The majority of patients find most freedom from dyspnœa propped up in bed in an almost sitting posture.

Cachexia is much more common in sarcoma than in other mediastinal tumors, but many patients maintain a surprisingly good state of nutrition. Moderate irregular fever occurs in a number.

Palpation yields additional data about thoracic deformities and pulsation. Palpation of the neck and axilla for tumor extensions or metastases is very important. Particularly is this true of the sternal notch. Here deep palpation may show a tumor mass in the upper mediastinum. It has even been suggested that a skin incision be made so that the palpating finger may reach more deeply into the retrosternal region. In a few cases enlarged lymph nodes can be palpated along the lower border of the pectoral muscle. Extension through the intercostal spaces rarely occurs. Excision and microscopic study of accessible metastatic or extension nodules will, in some cases, yield a positive diagnosis.

In all cases of suspected mediastinal mass the larynx should be palpated. In some cases it will be found fixed, no longer ascending and descending with deglutition and respiration. This is due to a mass pressing on the trachea and bronchi and fixing them. In other cases a tracheal tug, synchronous with the heart beat, will be found. This has been reported in mediastinal tumor, but is far more common in aneurism.

In a certain number of cases percussion of the thorax reveals no evidence of any tumor mass within the chest. In an occasional case where the tumor occupies the posterior mediastinum and produces no dulness anteriorly, percussion over the spines of the dorsal vertebræ may give an abnormal note, such as occurs in some cases of tuberculosis of the peribronchial lymph nodes, without there being any demonstrable dulness elsewhere in the back. However, in the larger number there is a localized area of dulness to be made out in the region of the manubrium sterni which gradually increases in size with the growth of the tumor. Not infrequently such an area of dulness shows not a smooth, rounded outline, but an irregular contour, suggesting a lobulated mass. Most frequently

the area of dulness is small, extending a short distance on either side of the manubrium, though it may be large, involving the greater part of the anterior thorax on one side. It may be apparent also in the back, and the two areas of dulness be separated by resonant lung. The fact that the outline of dulness, although extensive, nowise corresponds to the anatomical position of a lobe or lobes of the lung and does not occupy dependent portions of the thorax in most cases serves to distinguish the area of dulness so produced from one due to pulmonary consolidation, or fluid in the pleural cavity. Over the area of dulness, tactile and vocal fremitus is greatly decreased or absent. Auscultation of the dull area not infrequently is negative. In some cases, where there is dulness over the manubrium, there is an increased transmission of tracheal respiration; in others over the dull area breath sounds are distant or even absent. Auscultation of the chest outside of the area of dulness may reveal normal vesicular breath sounds, or one side of the chest may show suppressed breathing or almost total absence of respiratory sounds. In such a case there is pressure obstruction to the bronchus of one lung. On the other hand, auscultation frequently reveals numerous medium and coarse rales, often piping or sonorous in character, in one or both lungs, indicative of a more or less generalized bronchitis, resulting mainly from pressure.

In their growth, mediastinal sarcomas may involve various nerves. Pressure on the recurrent laryngeals produces paralysis of the vocal cords and is a common sequel; on the intercostals it causes an intercostal neuralgia, but this is infrequent. Pressure on the sympathetics may lead to unilateral sweating. More commonly the dilator of the iris is involved, with dilatation during the irritative stage, followed by constriction if the nerve bundles are destroyed. This latter with also an ulnar paralysis is shown by a case of Pfeiffer[1] where a mediastinal lymphosarcoma invaded the first and second left dorsal roots, producing a constriction of the left pupil and paralysis in the distribution of the ulnar nerve. Involvement of the phrenic nerve produces neuralgia in the course of the nerve, sometimes hiccough. With pressure on the vagus comes heart palpitation, possibly a slowing of the heart in some cases, cough, and gastric disturbances.

In a very few cases the tumor invades the spinal column and produces pressure on the spinal cord, as in the case of Poulain,[2] of a woman, aged thirty-one years, who for three years had had pain in the right side of the chest, intermittent dyspnœa, cough, and at times a blood-streaked expectoration. The superficial veins of the upper part of the right front of the chest were found engorged and the jugulars, especially the right, dilated. There was a severe paroxysmal pain radiating around the right side of the chest. About six weeks after admission, sensations of the body below the level of the umbilicus became diminished and there was a certain degree of paresis. In two weeks this had developed into anæsthesia and complete paraplegia of a flaccid, non-painful type. At autopsy a spindle-cell sarcoma of the mediastinum was found, which involved the fifth dorsal vertebra and extended into the spinal canal, compressing the cord.

Tumors in their downward growth may surround the heart and more or less impede its action. Sometimes the heart is almost completely surrounded

[1] *Deutsch. Zeit. f. Nervenheilk.*, 1891, i, 345.
[2] *Bull. Soc. anat. de Paris*, 1898, lxxiii, 623.

by tumor, as in a specimen recently shown by Sternberg.[1] That a heart should be able to continue pulsating under these conditions seems remarkable.

Some pressure on the lungs as the tumor grows laterally is constantly present, but direct symptoms from this are slight, even though the tumor occupy almost the entire pleural cavity. Very frequently associated with the tumor there is pleurisy with effusion, producing its ordinary symptoms.

Pressure on the trachea leads to stenosis, labored breathing, and stridor. Here respiratory rhythm in proportion to the dyspnœa is slow. The dyspnœa is either inspiratory, or both inspiratory and expiratory. Pressure on a single main bronchus, on the other hand, produces very little change in respiration, but there is a diminished activity of the corresponding lung evident on auscultation. The thoracic duct is rarely obstructed, as in a case of Matzinger[2] producing chylous ascites or hydrothorax.

**Diagnosis.**—The physical signs already described, taken in consideration with the symptoms, in most cases lead to the correct diagnosis of mediastinal tumor. Its nature, whether malignant or benign, is shown chiefly by the course of the disease and by the extent and rapidity of development of pressure symptoms.

If there is indication of a malignant tumor, it is, in the great majority of cases, a sarcoma. Radiographic examination of the thorax has been of great aid in the diagnosis of mediastinal affections. The shadow of a mass points distinctly to a mediastinal affection. The absence of a pulsating outline is against, although not excluding, an aneurism. When the contour and the shadow are irregular, there is very little probability of the mass being an aneurism and strong likelihood that it is a tumor. Radiographs taken from time to time indicate any progressive increase in the size of the mass, and when the growth is irregular the diagnosis is practically certain. Certain of the smaller tumor masses situated in the median line may escape detection, as their shadow is lost in that produced by the spinal column and the sternum. In these cases an oblique illumination may reveal what has escaped an antero-posterior one. Even without the aid of radiographs the diagnosis in most cases can be and is made antemortem. In a number of cases, however, the radiographs will give an earlier diagnosis and a clearer differentiation from aneurism.

In very few cases of mediastinal tumor is the radial pulse smaller on one side. This is very much more common in aneurism. Moreover, inequality of the radial pulses occurs in a number of other conditions, such as in an anatomical anomaly of the radial artery of one side, in old hemiplegias, in sclerosis more marked in one radial, in obstruction at the mouth of the artery by sclerotic processes in the aorta, and by any form of pressure obstruction in the course of the vessel. On the other hand, high-grade signs of venous obstruction point to neoplasm. Ekgren[3] has called attention to a blood-pressure phenomenon which he regards of value in diagnosing mediastinal tumors. This is a difference between blood pressure in the two brachials while in the dorsal recumbent position, not present while standing. Ekgren reports a case in which while lying on the back the blood pressure was 60 to 70 mm. lower on the right side. At autopsy a large mediastinal lymphosarcoma was found.

[1] *Centralbl. f. innere Med.*, 1906, xxvii, 25.
[2] *Buffalo Medical Journal*, 1901–2, xi, 755.
[3] *Fortschr. d. Medizin*, 1902, xx, 105.

Diagnosis from tumors of the lung is difficult, because tumors of the lung tend to invade the mediastinum early and many of the symptoms and physical signs, usually given in a consideration of tumors of the lung, are due to the mediastinal portion of the tumor. After the mediastinum becomes involved, it is often impossible to tell whether the tumor was primary in lung or in mediastinum. A history of onset with cough and blood-stained sputum without any evidence of pulmonary tuberculosis, particularly in a person over fifty years of age, strongly suggests a primary tumor of the lung. Portions of the tumor may be expectorated and be detected in the sputum. This is unlikely in mediastinal tumor. Localized dulness of a wooden quality suggests a tumor in the lung. Vocal and tactile fremitus is decreased over this region and breath sounds are usually weak, not bronchial, in character. In some cases of tumor of the lung a change of physical signs from a tympanitic to a dull percussion note during several days' observation, with a probable return to the original conditions later, occurs. This is due to a previously atelectatic portion of lung refilling with air as its bronchus becomes free. These signs in the absence of any evidence of considerable mediastinal growth (pressure symptoms) point to a primary tumor of the lungs rather than to a primary mediastinal tumor. Radiographic examination in some cases confirms the presence of a pulmonary mass without mediastinal involvement.

**Treatment.**—Little can be said with regard to treatment. Alleviation alone is possible medically. Pain, cough, expectoration, and dyspnœa may be symptomatically controlled; cure is not to be expected. Unfortunately, at the present time, surgery has but little more to offer in the case of malignant tumors. The art of intrathoracic surgery under the influence of the pneumatic chamber may, in the future, develop sufficiently to offer hope of cure for some of these cases. Still there is the chance of the tumor being benign in character, and possible of removal; consequently in the future surgical interference should be considered in these cases, and it is to be hoped that some advances may be made along these lines.

**Endothelioma.**—Only a few cases of endothelioma of the mediastinum have been reported. It is doubtful whether true endotheliomas arise from the mediastinal tissues. Those described probably have started from the pleural endothelium (mesothelium) and extended into the mediastinum. The symptoms produced in the mediastinum are those of other extensive secondary malignant growths there. With these are associated symptoms and physical signs due to development in the pleura.

**Carcinoma.**—As has already been pointed out, primary carcinoma is not, as has been very generally although incorrectly stated, common in the mediastinum. Aside from carcinoma arising from the œsophagus, trachea, and bronchi, the only epithelial structures in the mediastinum serving as possible sources for carcinomas are the thymus, misplaced or accessory thyroid, and fœtal remains separated in the development of the respiratory or alimentary tract. The thymus normally disappears before the age of proneness to carcinoma comes; intrathoracic thyroid more usually produces intrathoracic goitre and is considered in that connection; fœtal remains are excessively rare as a source. If we eliminate cases which should be classed as sarcomas, lymphosarcomas, secondary carcinomas, pleural endotheliomas, and bronchial carcinomas, few cases remain. Josephson, working under Baumgarten, collected 46 cases of so-called mediastinal carcinoma.

Only 11 of these were studied and described sufficiently well to apparently deserve the diagnosis according to Josephson and Hoffmann, who think that several of these 11 are wrongly included. Lohrisch[1] has collected the cases of mediastinal tumor reported in 1896–1901 and finds but 2 of carcinoma and 2 with allenomatous parts. A review of the latter shows them to be tumors of complex structure (adeno-chondro-sarcomas) and more closely allied to teratomas than carcinomas. Since 1901 the writer has been able to find the report of but one satisfactory case, that of Zypkin.[2]

The following is a typical example: The case of Kasem-Beck[3] was a man of sixty-four, who for two years had suffered from shortness of breath and attacks of pain in the sternum, radiating to the neck and upper extremities. Soon after the onset of pain a swelling developed in the right infraclavicular fossa. For a year there was bloody sputum. On admission to the hospital there were marked emaciation, cyanosis of the upper extremities and mucous membranes; scoliosis of the spinal column; exophthalmos of the right eye; slight œdema of the lower eyelid; swelling of the veins on the right side of neck. In the right supraclavicular fossa there was a series of enlarged lymph nodes and the infraclavicular bulged somewhat. The tumor in the former situation was movable, in the latter fixed. The apex of the right lung was depressed and there was dulness behind in the upper part of the right back, and in front over the manubrium and to the right with irregular outline. Over the area of dulness the respiratory sounds were weakened, but expiration was bronchial in type. A small tumor mass was removed from the infraclavicular fossa and microscopic examination showed it to be carcinoma. At autopsy a tumor occupied the anterior mediastinum which had penetrated the apex of the right lung and the pericardium. Metastases were present only in the lymph nodes of the right side of the neck and the inguinal region. The lumen of the superior vena cava was partly compressed near the pericardium.

In the cases reported by Paviot and Gérest,[4] Letulle[5] and Zypkin[6] the diagnosis was confirmed at autopsy. In several of the cases the evidence for the diagnosis seems unconvincing. Others were probably overlooked. Symptomatology based on such a small group of cases must be imperfect and is scarcely warranted. These cases, however, do show the tendency to occur in older people as would be anticipated for carcinoma. An invasive form of growth and the frequency of venous obstruction with localized œdema, cyanosis, and venous dilatation are to be regarded as points favoring the diagnosis of carcinoma rather than sarcoma and lymphosarcoma. However, before any very definite differential points can be given many more cases must be carefully studied during life and the diagnosis made certain by careful histological study after death.

**Simple Cysts.**—Although much more infrequent than dermoid cysts, simple cysts may occur in the mediastinum. Usually these have been small and lined by ciliated epithelium. Most of them are considered to have arisen from a fœtal misplacement of tissue associated with the development

[1] Lubarsch and Ostertag's *Ergebnisse d. allgemein. Path.*, etc., Anhang., 1900–1, vii, 912.
[2] *Wien. klin. Rundshau*, 1906, xx, 34.
[3] *Centralbl. f. innere Med.*, 1898, xix, 281.
[4] *Archiv. de méd. experiment. et d'anat. path.*, 1896, viii, 606.
[5] *Archiv. gén. de méd.*, 1890, ii, 641.
[6] *Loc. cit.*

of the œsophagus. A case of Westerynk[1] seems to have originated from the thymus.

Among the accounts of 12 cysts reported, it was found that 6 were situated in close proximity to the bifurcation of the trachea, 4 near the lower end of the œsophagus, and 1 in the anterior mediastinum 4 cm. above the tracheal bifurcation. Almost all of the cysts were small. In most of the cases the cyst produced no symptoms. In Fletcher's case, a girl aged six, there was cough for one week, dyspnœa, and cyanosis for three days before death.

Bramwell's[2] case is of interest because of the difficulties in diagnosis. It occurred in a man aged fifty with a history of syphilis and for several years a hard drinker. He entered the hospital on account of nephritis. It was then found that he had visible, palpable pulsation over the second right interspace near the sternum, localized dulness, and a slight systolic thrill. In this region a systolic murmur could be heard and the aortic second sound was accentuated. There was no pain and no pressure symptoms. Still the diagnosis of aneurism seemed justified. A year later he died from nephritis, and autopsy showed that the dulness was due to a cyst in the mediastinum. The pulsation was transmitted from the aorta. The accentuated second sound was associated with the nephritis. The systolic murmur came from a thickening of the aortic valves.

**Dermoid Cyst and Teratoma.**—Among the more uncommon tumors of the mediastinum are those which may be grouped together as dermoid cysts and teratomas. This group consists of tumors varying in complexity from a simple cyst lined by epidermis with its appendages (hair follicles, sebaceous glands, or sweat ducts) to solid tumors made up of a variety of tissues in complex arrangement. Between these two extremes all gradations of complexity are met and it is difficult so to define the terms, dermoid cyst and teratoma, that two distinct groups can be made. Furthermore, all have much in common as to origin, course of development, and symptomatology, and they can be best described together.

These tumors do not occur very frequently. Hare in 1889 among 288 cases of mediastinal tumor reports only 10 dermoid cysts. At the end of 1901 the writer[3] was able to collect 40 such cases, and recently Morris[4] has brought this number up to 57. To these are now added 2 unpublished cases, which with 5 additional from the literature increase the total to 64 cases from the first reported by Gordon in 1823 to the time of this analysis.

Notes of the unpublished cases are given below:

CASE I.—A woman[5] aged fifty was admitted to the Massachusetts General Hospital, February 1, 1897. For twenty years she had had a lump in her neck, which two years ago she opened with a pin and from it three or four spoonfuls of thick liquid escaped. Physical examination showed slight dulness under the sternum. There was a tumor the size of a small apple in the median line of the neck with its lower border near the sternal notch. It was

[1] *Prag. medicin. Woch.*, 1900, xxv. 373.
[2] *Clinical Studies*, Edinburgh, 1902–3. 145.
[3] *Journal of Medical Research*, 1902, vii, 54.
[4] *Medical News*, September 16, 1905.
[5] Specimen kindly given to me by Dr. J. H. Wright, Director of the Clinico-Pathological Laboratory of the Massachusetts General Hospital.

not adherent to the skin, fluctuated, and seems to have several small, hard lumps adherent to its wall. At operation (C. B. Porter) a semicircular incision was made about the lower edge of tumor and it was freed from the surrounding tissues. While doing this the tumor was punctured and a considerable amount of sebaceous material containing hair escaped. Further dissection showed a long process running down behind the sternum, communicating with an intrathoracic cyst from which hair and tissue were removed. This cyst was finally packed with gauze. On March 16th, Dr. Homans enlarged the incision above the sternum, cleaned out the retrosternal cyst, and packed it with iodoform gauze. The sinus gradualy filled up and the patient was discharged May 4th with the wound almost completely healed.

CASE II.—A boy[1] aged nineteen years came to the doctor on May 19th complaining of rapid emaciation and slight cough. The boy was effeminate in expression, manner, and voice. His breasts were large and full, with deep areolæ. His genitalia were well developed and normal. On July 19th he returned with a history of pain in the right side and renewed cough. There was almost total disappearance of the vesicular respiratory murmur, dulness, and almost complete absence of vocal fremitus over the entire right thorax. Pleuritic effusion was suspected, but repeated efforts to aspirate failed, the needle appearing to enter a solid, resistant mass. The boy had frequently passed segments of tapeworm and the parents became convinced that the tapeworm was responsible for the boy's condition. Accordingly, they had a "botanic" physician institute an energetic treatment, with the result that ten yards of tapeworm was passed on August 24th. Two days later the boy died with symptoms of exhaustion. An autopsy revealed a large tumor occupying nearly the whole of the right pleural cavity. The lung presented as a flattened lobe crowded into the posterolateral porton of the upper part of the pleural cavity. The right bronchus was embedded in the tumor. The heart was crowded over to the left in an almost horizontal position, and the left lung was somewhat compressed. The tumor weighed 4750 gms. The spleen was enlarged; the other viscera were normal. There were no tumor metastases. The tumor was lobulated, firm, grayish to pink in color, and contained many small cysts filled with a colloid material. Microscopic examination showed a stroma of connective tissue, smooth muscle, cartilage and neuroglia, containing small cysts lined by flat, cuboidal, or cylindrical epithelium, some ciliated and some of the mucous type. It was a teratoma.

CASE III.—A boy[2] aged seventeen, rugged, but free from any previous serious illness. There had been slight cough at intervals for two or three years and the patient had been run down and unable to go to school since December, 1904. He had slight dyspnœa and a husky voice for six months, but no increased cough and no pain. The thorax on the right side was fuller than on the left and the respiratory movements were reduced; there was flatness on the right side below the second rib out to the anterior axillary line, and continuous with the hepatic flatness below and cardiac flatness to left. Respiratory sounds and tactile fremitus were absent over this area. In the right axilla there was an almond-sized lymph node.

[1] Specimens sent to the writer by the late Dr. J. M. Sheahan, of Quincy, Mass.

[2] Griffin, *Boston Medical and Surgical Journal*, 1907, clvi, 9. The patient was seen in consultation with Dr. W. A. Griffin, Sharon, Mass.

On tapping, about two ounces of thick fluid were obtained, which was amorphous and cultures from it negative. Next day about two inches of the sixth rib were resected in the right midaxillary line and the pleural sac opened. A small amount of the same fluid was obtained. A tense tumor mass presented, moving with respiration and unattached to the diaphragm below. This was opened, with the escape of considerable fluid. The finger introduced into the opening could feel three or four sessile, non-movable, grape-like projections. There was free drainage of a fluid containing numerous small, pinhead and larger, bright-yellow granules, sometimes showing a radiate structure. In a few, short, pale, tapering hairs were embedded. The diagnosis of a dermoid cyst of the mediastinum, extending into the right thorax, was made. The tumor was partially removed at operation and the solid portion proved to be of complex structure in places showing rapid proliferation. The patient died some months later.

Dermoid cysts and teratomas in the mediastinum, as elsewhere, probably originate early in fœtal life, although their active growth does not come until early adult life. Many of the tumors in this region, either by position or structure, show a developmental relation to tissues whose origin is associated with the formation and disappearance of the branchial clefts of the embryo; their origin is branchiogenic, with descent into the mediastinum during fœtal development. Others appear to have originated from tissues misplaced at the time of closure of the anterior chest wall. Those of greatest complexity are perhaps best explained as fœtal inclusions. However, these are but tentative theories of genesis which serve for the present to give a clearer understanding of teratoid tumors in this region; the true solution of their origin must wait until we have an adequate insight into the formation of complex tumors in general.

Structurally we can roughly subdivide these tumors into three classes: (1) Cysts of slight complexity; these are essentially dermoid cysts of ectodermal origin. (2) Tumors of great complexity; these contain derivatives of all three germ layers and may be regarded as teratomas. (3) Tumors of the first or second class, which, in some part of their structure, show a malignant character and form metastases.

In the first group are simple unilocular cysts, unilocular cysts with diverticula of varying size, and multilocular cysts. The cysts are either smooth or contain polypoid excrescences of greater or less complexity. Their walls are lined by epidermis containing as a rule hair follicles and sebaceous glands, less frequently sweat ducts. The walls may contain bone (13 cases) or cartilage (18 cases), or both. Not infrequently teeth are present (8 cases). In some, besides the large cyst, smaller cysts lined by simple cylindrical or ciliated epithelium occur. In the cases of Marchand[1] and Pinders there were structures resembling thymus, while in Mandlbaum's case thyroid vesicles were found.

The tumors of the second group (6 cases) are more solid structures, made up of small cysts lined by a variety of epithelia with an intervening stroma of connective tissue containing bone, cartilage, smooth muscle, etc. In 2 of the writer's cases masses of neuroglia were found. Of the last group only 4 cases have been reported. Pinders' case was in part lymphosarcoma, Jores' spindle-cell sarcoma, Virchow's both carcinoma and sarcoma, and Bull's a solid teratoma with elements of the central nervous system.

[1] For original source of this and other cases, see paper of Christian or Morris.

The content of the cyst in almost every case is a greasy, gray to yellow, semisolid material in which hair is mingled. In size they vary from a pigeon's egg to a tumor larger than a child's head.

The primary position of the tumor is usually in the upper half of the thorax, wholly or in part immediately behind the manubrium sterni. A smaller number are situated in the lower half of the thorax, between the heart and the adjacent lung. In several cases the tumor appeared in the neck in the suprasternal notch or above the sternoclavicular articulations. In the upper part of the anterior mediastinum, where they more usually occur, there is a potential space between the sternum in front and great vessels behind capable of accommodating a medium-sized tumor. Development of the tumor beyond a certain point in this region would be resisted in front by the bony wall of the thorax, and behind by the great vessels and trachea supported by the vertebral column. Growth would be possible in three directions—upward through the superior aperture of the thorax, laterally into the pleural cavity, and downward between the heart and lungs—and these three directions of expansion occur in reported cases.

For some tumors not situated in the upper anterior mediastinum, a previous position there can be assumed. Portions of some of the largest tumors, the greater part of which lies in the pleural cavity, still extend into the upper mediastinum, and it would seem probable that with them a change of position has taken place along lines of least resistance merely to accommodate their bulk adequately. In other cases there is structural proof of development in the upper mediastinum and subsequent migration. For some a primary development in the lower mediastinum cannot be excluded.

In almost every case adhesions to some adjacent organ occur. The tumor is most frequently bound to some part of the lung and almost as often to the pericardium. Less frequently they are attached to other structures, as chest wall, diaphragm or great vessels. These tumors, though occupying a position surrounded by vital organs and generally in actual union with them do not as a rule produce great destruction of adjacent structures. In one case the aorta was eroded, in a second there was a communication between the tumor and the pericardial cavity; in a number of cases they eroded into the lung and formed a communication with the bronchus.

**Age.**—These tumors are far more frequent in young adults. Of the reported cases nearly 62 per cent. came to observation between the ages of eighteen and thirty years. The 50 cases in which the age is given are divided between the decades as follows:—

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Between | 1 | and | 10 | years | ..... | 5 | cases. |
| " | 10 | " | 20 | " | ..... | 7 | " |
| " | 21 | " | 30 | " | ..... | 25 | " |
| " | 31 | " | 40 | " | ..... | 6 | " |
| " | 41 | " | 50 | " | ..... | 3 | " |
| " | 51 | " | 60 | " | ..... | 3 | " |
| " | 61 | " | 70 | " | ..... | 1 | " |

Sex has no apparent influence on their occurrence.

**Symptoms.**—The onset of symptoms in cases of dermoid cyst or teratoma of the mediastinum is nearly always gradual. There is usually a latent period during which the tumor gives no evidence of its existence. Ordinarily this continues up to the time of puberty. Then the tumor begins to grow more or less rapidly and as it increases in size it begins to press on

adjacent structures and symptoms appear. This constitutes a period of activity. While this is true of most cases, in others symptoms have appeared at an earlier or later period or the tumor remained latent throughout life, to be an accidental finding at autopsy.

The onset of an active stage is by no means characteristic. Indeed, it is seldom that the condition has been correctly diagnosed early. The most common earliest symptom is dyspnœa after exertion, frequently associated with pain in the chest, at times with cough or a feeling of pressure. Less commonly pain and hæmoptysis have been the initial symptom. With progress of the growth of the tumor, dyspnœa almost always becomes prominent. In the earlier stages it is apt to be intermittent, greatly aggravated by exertion, and generally accompanied by cough with expectoration, frequently blood-tinged. In the later stages difficult breathing is more constant and severe, and it may become so extreme as to cause death. Dysphagia does not occur.

Pain is a frequent symptom, although it may be slight and often is not present at all. The pain is usually sharp, seldom dull and aching. In a certain number of reported cases the pain has radiated to the shoulder (8 cases) or to the back of the head (2 cases). There is nothing typical in the cough. The expectoration, however, is of very great importance in the diagnosis and should be carefully examined in every suspected case. The quantity varies greatly; at first it is small in amount, but later may become very copious. The sputum may be divided into two groups: that which comes merely from the bronchi and that which comes from bronchi and cyst cavity by way of a perforation into a bronchus. The first is in no way characteristic; it results from the bronchitis following pressure of the tumor on the trachea or bronchi; it is the sputum of a chronic bronchitis and is apt to occur with any mediastinal mass. The second may be characteristic and in some cases is pathognomonic. Search should be made for epithelial cells, resembling those from the horny layer of the skin, for fat droplets, fatty acid and cholesterin crystals, and for hairs. The finding of the latter is absolutely diagnostic, the others highly suggestive of dermoid cyst. It is not likely that the sputum will aid in the diagnosis of a solid teratoma. In 21 of the reported cases there has been a communication between the cyst and a bronchus. In 11 of these, hair was expectorated and 8 were correctly diagnosed.

Hæmoptysis is quite common. Usually it is a late symptom. It may be severe enough to cause death (5 cases). In other cases there is continued but slight loss of blood, so that the sputum is almost always blood-tinged.

The course of the disease is relatively a slow one, a period rather of years than of months. This is in strong contrast to cases of malignant disease of the same region. Reported cases with sufficient data for determining the duration may be grouped as follows:

| | | | | | | |
|---|---|---|---|---|---|---|
| Duration of | less | than | 1 | year | 3 | cases. |
| " | 1 | to | 2 | years | 7 | " |
| " | 3 | to | 5 | " | 10 | " |
| " | 5 | to | 10 | " | 5 | " |
| " | 10 | to | 15 | " | 2 | " |
| " | more | than | 15 | " | 2 | " |

Dangschat divides the cases into three groups: those with insidious onset and gradual constant increase in severity of symptoms; those with similar

onset, but with sudden development of severe, often fatal symptoms; those with severe symptoms at the beginning and a later course of remissions and exacerbations. To these may be added a fourth group: those latent throughout their course.

**Physical Signs.**—The patients are usually well nourished and show no evidence of cachexia. The superficial veins of the thorax are not distended. There is no local œdema. The radial pulse is equal on the two sides. In no case has paralysis of the vocal cords been noted. Frequently the tumor produces a fulness or bulging of the chest wall, usually anteriorly. This is oftenest in the upper part of the chest from the level of the second to the sixth ribs, but may be elsewhere, as in v. Török's case, where it occurred low down posteriorly. This asymmetry of the chest persists for months or years, showing little or no change in size. The tumor may appear in the neck through the superior aperture of the thorax (7 cases), and in some of these fluctuation can be made out. In others pulsation may be present, but is not expansile in character. Fistulous communication between the cyst and skin surface may form with discharge of characteristic cyst content.

If the tumor is of moderate size, percussion almost always reveals an irregular area of flatness or dulness over which breath sounds and vocal and tactile fremitus are diminished. This is practically always the case when the tumor deforms the chest and corresponds to the prominence. The dulness usually begins high up in front and extends downward and outward. Its upper border may resemble the upper border of a pleurisy with effusion, except that the curve is reversed in direction. In some cases the dulness is situated behind. Again, there may be dulness anteriorly and posteriorly with intervening resonance, or almost the entire right or left half of the thorax be dull. Very frequently moist or dry rales are heard throughout the lung on the side of the tumor, not infrequently on both sides. Where the tumor is large or situated low down, displacement of the heart occurs or the liver may be pushed downward.

**Diagnosis.**—When hairs are expectorated, or escape from a fistulous communication with the skin, the diagnosis offers no difficulty. Fat droplets, fatty acid and cholesterin crystals or squamous epithelium similarly escaping from the cyst give a good clue to the diagnosis. Exploratory puncture has yielded a correct diagnosis in some cases. In several cases puncture has been made under the impression that pleurisy with effusion existed. The *x*-ray examination, besides showing the situation of a tumor mass, may reveal the nature of the tumor, when bone or teeth form a part of the growth, although no such case has yet been reported.

A probable diagnosis can be made when we have evidence in a young adult of a mediastinal tumor of slow progress. The duration of malignant disease is rarely as long as one year. Cachexia common in malignant disease is rare in dermoid cysts and teratomas. Pressure signs such as œdema, cyanosis, distention of superficial veins, inequality of the pupils, and laryngeal changes, are not found in connection with mediastinal tumors of this group, except in those more infrequent ones which show malignant parts. The course of the latter is like carcinomas and sarcomas, and, like them, dermoid cysts and teratomas are proven malignant when there is evidence of metastasis.

The diagnosis from aneurism is usually not difficult A case similar to Buchner's, where there was a communication between cyst and aorta, would

of course present diagnostic difficulties, but such a condition is little to be expected and, if it occurred, the treatment would be that of aneurism, for such it was practically. Echinococcus cysts can be differentiated from dermoids only by an examination of their contents. Other benign tumors are rare, and inflammatory processes present almost no difficulty.

**Prognosis.**—Prognosis as compared with that of malignant tumors is good, since the latter are almost invariably fatal in less than one year, but it is to be remembered that, unless operated on, the chances for life for more than a few years are not very good.

**Treatment.**—Surgery presents the only hope of cure. Medical treatment other than palliative is futile and every patient should be given the chance of surgical treatment. In these cases radical operation is rendered difficult by the proximity of vital organs, the frequency of extensive adhesions, and the danger of entering the pleural cavity with the production of a pneumothorax. Simple drainage often proves ineffectual, owing to the cyst being multilocular or to the presence of diverticula in a simple cyst. Yet modern surgery has very largely overcome these difficulties, and of 20 cases operated on, including those of early date, 70 per cent. were much benefited and a considerable number cured. Although the operation is a serious one, yet the results to date justify an attempt at removal in every case and offer a reasonable hope of complete cure. Every patient with dermoid cyst or teratoma of the mediastinum, once diagnosed, should be promptly sent to the surgeon.

**Intrathoracic Goitre.**—The thyroid gland may have a low position and the isthmus and lower part of the lateral lobes lie behind the manubrium or sternal ends of the clavicles. Occasionally there are accessory glands lying in the mediastinum. Hyperplasia under these conditions leads to the formation of intrathoracic goitre or tumors benign or malignant may here develop. In this case symptoms of intrathoracic pressure arise. Wuhrman[1] collected 75 benign and 16 malignant growths of this class, so they form an important group. However, their consideration belongs more properly under diseases of the thyroid. It is important here to call attention to their occurrence, to the advisability for surgical treatment, and the frequent presence in such cases of a palpable strand of tissue connecting the intrathoracic mass with the thyroid. The latter is of great diagnostic importance.

## Secondary Tumors in the Mediastinum.

Tumors of various organs may metastasize in the mediastinal lymph nodes and tissues. This is true of all forms of malignant tumors and in this group might be included the enlarged lymph nodes of leukæmia and Hodgkin's disease. With the exception of the last, the metastases are usually small and their presence gives no symptoms. When they are large the symptoms are the same as those produced by the primary tumors and need no further discussion. The most common mediastinal metastasis is from carcinoma of the breast and from the breast the tumor may also reach the mediastinum by direct extension. A very common mediastinal exten-

[1] *Deut. Zeit. f. Chir.*, 1896, xliii, 1.

sion is from tumors of the lung or pleura. In symptoms and physical signs these closely resemble primary mediastinal tumors and are very difficult of diagnosis from them.

## MEDIASTINITIS.

Inflammation is not infrequent in the mediastinum, but, on the other hand, mediastinitis is not often recognized. This is due to the fact that most often the mediastinal inflammation arises as a complication of some process elsewhere in the body, whose symptoms mask those of the mediastinitis itself.

Inflammation in the mediastinum may be acute or chronic. In the acute there may be simply exudation, serous, fibrinous, or purulent, into the loose areolar tissue, or tissue disintegration may take place with abscess formation. No sharp line can be drawn between the two types; whether the one or the other occurs, depends on the cause, duration, and severity of the process.

For this reason in considering acute inflammation of the mediastinum it does not seem advisable to consider separately simple mediastinitis and mediastinal abscess, but they will be discussed together as stages of mediastinal inflammation, the former mild, the latter severe, their symptoms varying chiefly in degree. In chronic mediastinitis there may be connective-tissue proliferation with mediastinal adhesions or chronic abscess, the latter almost always tuberculous in origin.

**Acute Mediastinitis.**—This, whether in form of infiltrating exudation or abscess, occurs in the loose areolar and fatty tissue which surrounds the mediastinal organs. The seriousness of inflammation in this region depends on the facts that the mediastinum is a closed space structurally difficult of drainage either by nature or operative means, and that extension into vital structures is apt to take place owing to their close proximity.

Acute inflammatory processes in the mediastinum may be divided on an etiological basis into three groups—traumatic, extension, and metastatic. Of these the traumatic is the most important not on account of its frequency, but because trauma so often leads to abscess formation rendering this group of cases most serious. Inflammation by extension is more common, but in many cases, apart from the severity of the primary disease, is of no very great importance, at least in the acute stages. Metastatic inflammation in the mediastinum is the rarest of the three.

Blows on the chest, particularly over the sternum, with or without fracture of bones, frequently cause diffuse suppurative mediastinitis or mediastinal abscess. Goodhart[1] reports an instance in which, following a blow on the chest from a log of wood, pain in the chest and great dyspnœa developed, with a fatal result in six days. Autopsy showed purulent infiltration of the mediastinum, with double pleuritis and pericarditis. A somewhat similar case (Walker[2]) followed a blow on the chest by a red-hot bar of metal. This patient recovered.

Crushing injuries to the chest or spinal column, if not immediately fatal, sometimes produce this condition, as in an instance at the Boston City Hospital, in which, with suppuration of the tissues of the forearm about a Colles'

[1] *Transactions of the London Pathological Society*, xxviii, 1877, 37.
[2] *Lancet*, 1884, i, 17.

fracture and a fracture of the twelfth dorsal vertebra, there was an abscess of the mediastinum. The tissues of the anterior mediastinum were matted together, quite firmly attached to the sternum, and infiltrated with pus, which was most abundant at the level of the third costal cartilages. The pruulent fluid extended down between the pericardium and the right pleura.

Sometimes trauma appears to be the cause when there is little evidence of direct injury to the thorax. Such an example is given by Laird[1] in a man who fell out of an apple-tree several days before coming to the hospital. This fall gave him a thorough jarring, but did not cause any evident local injury. Severe pain in the neck, head, and chest developed later and the region about the sternoclavicular joint became swollen, reddened, and œdematous. Incision over this evacuated about a pint of pus from the anterior mediastinum. Complete recovery followed.

Penetrating wounds of the mediastinum, with or without injury to the trachea or œsophagus, form another group of cases in which mediastinal inflammation results. Günther reports a mediastinal abscess following a dagger wound penetrating the sternum.

Traumatic injury or perforation of the œsophagus, trachea, or bronchi by a foreign body is apt to produce mediastinal inflammation. Similar results may follow instrumental perforation during operative procedures, as in passing sounds in the œsophagus, as in a case reported by Hacker. In this case the communication between the œsophagus and mediastinum was demonstrated by an ingenious test. Gauze impregnated with a 2 per cent. solution of potassium ferrocyanide was inserted in the cavity through the drainage wound, and the patient then swallowed a small amount of 2 per cent. solution of citrate of iron. The gauze was then removed and found to be blue where the two solutions came in contact, thus demonstrating the opening in the œsophagus and also indicating its location. The course of healing was followed by the same means until it was evident that the œsophageal opening had closed. This happened fourteen days after the operation.

In the group of inflammations by extension come the very numerous cases where in pneumonia the mediastinal tissues are infiltrated with serum or seropus. This condition is frequently seen at autopsy, but the mediastinitis usually gives little or no indication during life of its presence as a complication and it is rare for it to go on to abscess formation. In cases of this group coming under personal notice, not infrequently adhesions were found at some point between the anterior border of the lung and the mediastinal tissues, the result of some previous pulmonary or pleural affection, and at this point there was a direct extension of the inflammation from lung to mediastinum. However, extension of an acute pleuritis secondary to the pneumonia is perhaps more common, and any inflammatory condition of the lung, as abscess, gangrene, tuberculous cavity, etc., can so act. Cases of pneumonia complicated by pericarditis or peritonitis very frequently show also mediastinitis, probably extending from the complicating lesions rather than from the primary pneumonia.

The tendency of an acute pericarditis to extend to the mediastinal tissues is well recognized and is not an uncommon postmortem finding. In some cases of general peritonitis without pericarditis or pleuritis there is an associated inflammatory infiltration of the mediastinum, probably the result of a lymphatic extension through the diaphragm.

[1] *Albany Medical Annals*, 1904, xxv, 657.

Any ulcerative process in the trachea, bronchi, or œsophagus tends by extension or by perforation to produce mediastinitis. Hacker gives an example where inflammation extended from a superficial ulceration of the œsophagus, following the use of the œsophagoscope, to the mediastinum, with abscess formation. This is particularly true of perforation of the œsophagus owing to food particles escaping and infecting the surrounding tissues, frequently causing abscess.

Inflammation of the mediastinal lymph nodes, if the nodes soften and break down, may lead to extensive inflammation of the mediastinum. This more commonly follows tuberculosis of the lymph nodes and the abscess is apt to be chronic in nature.

Acute osteomyelitis of the sternum, ribs, or vertebræ may be the starting point for mediastinal inflammation.

From the neck inflammation may extend into the mediastinum. From the superficial tissues of the neck this is rare, since the downward path of the process is well guarded by fasciæ, as can be demonstrated by injection experiments on the cadaver. From the tissues about the larynx and trachea, on the other hand, extension is easier, while along the prevertebral region it is almost the rule in extensive processes, except from those in the immediate subcranial region and about the upper cervical vertebræ, where lateral extension is commoner. Inflammatory conditions of the pharynx, larynx, trachea, œsophagus, and lower cervical vertebræ are apt to extend to the deep cervical tissues and from them may descend into the mediastinum. The primary causes of these are many. As an example may be given a case at the Boston City Hospital, where following measles and diphtheria there was a perforation of the larynx just below the rima glottidis. Behind the larynx and trachea there was a cavity 7 cm. long, about which the tissues were soft and necrotic. Through the middle of the cavity the œsophagus passed as an intact tube. In the anterior mediastinum was an area of suppuration 4.5 cm. wide, extending from the third to the sixth costal cartilage. The sternum at the level of the fourth costal cartilage was eroded and the fourth and fifth cartilages on each side were separated from the sternum. At this point the pus had infiltrated the subcutaneous tissues over the sternum.

Another case of this type died at the Long Island Hospital, of chronic pulmonary tuberculosis. During life a cervical abscess had been freely drained. At autopsy there was a drained abscess cavity in the left anterior inferior triangle of the neck. The inner one-fourth of the left clavicle had been removed. From the cavity in the neck there was an extension of the process downward along the side of the trachea into the mediastinum, where there was a drained cavity 5 cm. in diameter bounded on the left side by pleura. There was no communication between these cavities and the lungs, œsophagus, or trachea.

Solomon[1] gives a case in which, following a lateropharyngeal abscess, an abscess developed in the region of the thymus and extended down to the anterior surface of the pericardium, and this proved fatal. Rustizky[2] had a case starting from a periostitis of the lower jaw. Deep cervical cellulitis in which the beginning point is not clear (Ludwig's angina) may lead to mediastinal abscess as in another Boston City Hospital case where, following

[1] *Bull. et mém. de la Soc. anat. de Paris*, 1902, lxxvii, 903.
[2] *Centralbl. f. Chir.*, 1887, xiv, 902.

a purulent infiltration of the deep tissues of the neck, there was extension into the posterior mediastinum. The tissues behind the aorta were thickened, œdematous, and grayish in color, and those behind and about the trachea were also thickened and filled with a yellow, creamy pus.

Metastatic inflammation of the mediastinum may occur as a complication or sequel of a variety of infectious and pyæmic conditions. Cases have been reported during or following erysipelas, variola, typhoid fever, septic endocarditis, acute rheumatism, and other diseases. Examples of these are cited by Hare and by Hoffmann.

Notwithstanding this variety of possible causes a number of cases of mediastinal inflammation have been reported whose etiology is by no means clear. As in other regions of the body, we regard them as probably infections whose portal of entry is not discovered.

**Chronic Mediastinitis.**—Following the diffuse infiltration of an acute mediastinitis, granulation tissue may form, resulting finally in scar tissue, binding together the mediastinal structures and interfering with their function. This is especially likely to take place in association with pericarditis and produce a mediastino-pericarditis. Rarely, if ever, are the digestive or respiratory tracts interfered with by such a chronic process. Occasionally the veins are obstructed and very infrequently the thoracic duct. A case illustrating the latter is given by Comey and McKibben,[1] in which from chronic tuberculosis involving the apex of the left lung the process extended to the mediastinal tissues and involved the thoracic duct in scar tissue with consequent obstruction. Chronic abscess, practically always tuberculous in origin, is an extension process from broken-down bronchial lymph nodes or carious bones. Usually from the former abscess of the anterior mediastinum arises. Tuberculosis of the sternum and anterior ends of the ribs leads to disease of the anterior mediastinum, while from dorsal Pott's disease comes abscess of the posterior mediastinum. Chronic abscess pathologically differs in most respects but little from acute abscess; clinically, except for longer duration and less marked febrile disturbance, they are similar and the symptoms of the two will be considered together.

Abscess of the mediastinum, whether acute or chronic, after remaining localized for a time, is apt to rupture either into some of the mediastinal organs or on the skin surface. Perforation into the œsophagus may occur and the pus be vomited, or into the trachea or bronchi and the pus be coughed up or inspired into the lung. Extension to the pleural cavities is common and penetration of the pericardium may take place. Rupture into the aorta (Burk[2]) or large mediastinal veins has been reported. In a number of cases the pus reaches the body surface along the upper border of the sternum or it may burrow for some distance in the deeper tissues and reach the surface at various points on the thorax. In a woman aged thirty-five, reported by Ballance,[3] after many weeks of pain, a lump formed over the upper part and left side of the sternum from which pus was evacuated. A sinus persisted for two months, accompanied by severe pain and fever. The skin over the front of sternum and for eight inches beyond its left border became red, œdematous, and apparently undermined. A sinus extended to the second left sternocostal articulation, where there was bare bone. Finally,

[1] *Boston Medical and Surgical Journal*, 1903, cxlviii, 109.
[2] *Medico-Chirurgical Transactions*, 1846, xi, cited by Hoffmann.
[3] *Lancet*, 1888, ii, 857.

the sternum was trephined, freely opened, and drained. Recovery was rapid and complete. Sometimes the mediastinal suppuration extends to the neck and the abscess may rupture in the region of the sternal notch or the sternoclavicular articulation.

Obviously in conditions with so various an etiology as mediastinal inflammations, sex or age are of no special import in symptomatology. As might be expected, where trauma plays an important role in etiology, males more often are affected, and the young rather than the old, but no very striking age preponderance is found.

**Symptoms.**—Symptoms of mediastinal inflammation vary with the extent and character of the process. Many times inflammation exists in the mediastinal tissues associated with inflammatory conditions elsewhere, without there being any symptoms pointing to the mediastinal process. In acute inflammatory conditions, thoracic pain is the most common symptom and this is usually of a throbbing character. With this, fever, a rapid pulse, and the facies of any septic process are associated. With simple infiltration, pressure symptoms are not common, but with abscess formation, whether acute or chronic, they develop and there is a varying combination of dyspnœa, dysphagia, venous obstruction, and pressure on nerve trunks, with the train of symptoms already discussed under tumors. Pain due to nerve-root pressure may lead to errors in localizing the process, as where pain on the intercostal roots is referred to their terminals and the pain appears to be localized in the anterior mediastinum or with involvement of brachial roots the pain is localized in the arm.

In lesser degrees of involvement, physical signs of the condition are lacking unless, as frequently happens, there is extension to the skin surface, with localized redness and induration, with or without ulceration and sinus formation. Such extension usually takes place in the upper intercostal spaces near the sternal margin. It may appear over the sternum, especially at the junction of the head and body. In the suprasternal notch or above the sternoclavicular joint is another site. More rarely penetration takes place behind in the region of the spinal column. Dulness may be elicited on percussion. With larger collections of pus, Hacker has called attention to a shifting or disappearance of this dulness with change in the patient's position. More probably this sign will be given by cases in which, with perforation of the œsophagus or respiratory tract, there is a mixture of air and pus within the mediastinum. There may be bulging of the chest wall, fluctuation, or even pulsation synchronous with the heart beat. In a few cases mediastinal tumor or aneurism is closely simulated.

The course of mediastinal inflammation is usually rapid. Generally it is an acute condition developing in a few days, and extending over a short period only. More rarely it develops slowly over a period of weeks. The latter cases are often tuberculous in origin.

**Diagnosis.**—Diagnosis depends largely on the combination of symptoms of mediastinal pressure with general symptoms of a septic process. Abscess of tuberculous origin presents most difficulty. Where there is extension of the process to the skin surface the diagnosis is usually easy. In connection with these cases it is well to bear in mind that in some cases of mediastinal tumor there is fever unaccounted for by any secondary inflammatory condition, although the latter may be present, as in a Boston City Hospital case of extensive lymphosarcoma of the anterior mediastinum.

In this case perforation of the left primary bronchus had taken place. The tumor masses showed hemorrhage, and on microscopic examination there was much fibrinous and leukocytic infiltration of the tumor, so that many sections appeared to be from an inflammatory rather than neoplastic process.

**Treatment.**—Treatment is purely surgical. In the earlier stages poultices may aid; when pus forms evacuation is called for. For pus in the anterior mediastinum operation is relatively simple, in the posterior mediastinum access is much more difficult. A discussion of operative methods is beyond the domain of the present consideration.

## ECHINOCOCCUS CYSTS OF THE MEDIASTINUM.

Echinococcus cysts occur in the mediastinum, but are very rare. Hare tabulates 8 cases; Hoffmann 4 cases. Of Hare's cases only 1 was accessible. This (Habersohn[1]) seemed incorrectly included, since it was a cyst of the lung rather than of the mediastinum. Further, the criteria of diagnosis both before and after death appeared insufficient and the case might well have been one of tuberculosis. Hoffmann's cases are cited from Marfan, and all appeared in the older French literature the originals of which the writer has not been able to see. A single case will serve as an example of this condition. Rose[2] describes an echinococcus cyst perforating the thoracic wall in a woman aged twenty-five who had always been healthy. Six years before admission to the hospital she had noted a small lump about the size of an acorn just above her right breast. On admission this lump measured three inches in diameter. It was hemispherical, tense, elastic, and fluctuating. It lay over the sternal ends of the right second and third ribs beneath the fibers of the pectoralis major muscle, unconnected with the breast. An incision was made over the mass. During dissection the cyst ruptured, with the escape of clear colorless fluid. The cyst was found to communicate with a cavity in the anterior mediastinum which could contain 10 ounces of fluid. From this both scolices and daughter-cysts were obtained, making the diagnosis certain. The inner membrane was removed from the cavity and it was packed with gauze. The patient recovered and the wound healed. Notwithstanding the large size of the mediastinal portion no symptoms had been produced.

## ABNORMAL MEDIASTINAL CONTENTS.

**Hernia.**—A rare condition is hernia of abdominal viscera through the diaphragm into the thoracic space. Congenital defects of the diaphragm in the stillborn or in those dying soon after birth are the commonest cases. In such cases the abdominal viscera more commonly occupy the pleural than the mediastinal space. Hernia of congenital origin also occurs in the adult, but is more usually associated with some injury or strain of the diaphragm. Just behind the xiphoid cartilage the diaphragm is structurally weak. Here and behind, where there are openings in the diaphragm for the passage of vessels and the œsophagus, herniæ are prone to occur, with the entrance of abdomi-

[1] *Guy's Hospital Report*, series 3, xviii, 373.
[2] *Lancet*, 1893, ii, 1308.

nal viscera into the anterior or posterior mediastinum, respectively. The stomach and colon are the organs more commonly concerned. These cases may be symptomless. Nausea and vomiting may be associated with displacement of the viscera or there may be symptoms of pressure on the mediastinal structures. The presence of gurgling sounds in the mediastinumis the physical sign of most aid in diagnosing this condition. Death from intestinal obstruction in these cases is not uncommon. Surgical interference offers the only chance of relief.

**Hemorrhage.**—Slight mediastinal hemorrhages may occur in purpura, the hemorrhagic exanthemata and other severe infectious processes. Severe hemorrhages are of traumatic origin or due to the rupture of aneurisms. If the person survives the immediate injury, the blood is gradually absorbed without any harm. In some cases of considerable hemorrhage there are pressure symptoms.

**Emphysema.**—Emphysema is a rare mediastinal lesion. Air may enter the mediastinal tissues as the result of trauma of the thorax; tracheotomy; ulceration of the œsophagus, trachea, or bronchi; pertussis; or pulmonary disease. Usually there is a history pointing to some one of these causes. Physical examination in these cases shows partial or complete absence of cardiac dulness and in its place a tympanitic percussion note. Cardiac pulsation is neither visible nor palpable. The heart sounds are muffled. Synchronous with the heart beat there are fine crackling sounds, usually systolic in time, sometimes both systolic and diastolic. Usually there is also an accompanying emphysema of the neck, more often on the left side, and possibly of parts of the thorax. In most cases there is respiratory distress and often dysphagia.

Mediastinal emphysema is to be diagnosed from pneumothorax and pneumopericardium. In pneumothorax the heart is displaced and the cardiac impulse can usually be made out in an abnormal position. In both pneumothorax and pneumopericardium the fine crackling sounds synchronous with the heart beat are absent and there is no accompanying subcutaneous emphysema. With mediastinal emphysema the metallic tinkling sound is not present and there is no change in the position of the area of tympany with change of position. Mediastinal emphysema in itself is not a serious condition and the air is readily absorbed. In many instances it accompanies a serious condition and may be a terminal event. The emphysema requires no treatment.

## DISEASES OF MEDIASTINAL LYMPH NODES.

For clinical purposes the mediastinal lymph nodes may be divided into three groups: the anterior mediastinal lymph nodes, those situated in the areolar tissue adjacent to the sternum and costal cartilages; the peribronchial lymph nodes, those lying about the primary bronchi and in the peribronchial tissue at the hilum of the lungs; the posterior mediastinal lymph nodes, those lying anterior to the vertebræ, about the aorta and œsophagus. Further anatomical subdivision is not required for the purposes of the present consideration.

Of diseases of the mediastinal lymph nodes, tumors have already been considered in connection with the general subject of mediastinal tumors,

and abscesses of lymph-node origin were discussed under mediastinitis. There remain simple hyperplasia, pigmentation, sclerosis, and tuberculosis. These will be considered in certain particulars of local import aside from general diseases of the lymph nodes and tuberculosis described elsewhere.

**Simple Hyperplasia.**—In a variety of conditions the mediastinal lymph nodes become moderately enlarged. Their consistence is rather softer than normal. The cut surface is gray or pinkish-gray, provided the color is not obscured by carbon pigmentation. These changes are due to the action of bacteria or toxic substances, and are associated with lesions of the territory drained into the mediastinal lymph nodes or with general conditions affecting the lymph nodes of the body. Acute lesions of the lungs, pleura, and pericardium lead particularly to these changes. The peribronchial group is more often affected in this way, although both the anterior and posterior mediastinal group may be. As a rule these changes produce no symptoms. Occasionally in children, with repeated or prolonged attacks of bronchitis, there is considerable enlargement of the peribronchial lymph nodes, enough to produce pressure on the bronchi and irritation of the bronchial mucous membrane. This causes cough which is often stubborn, tends to be paroxysmal, and is apt to occur for the most part at night. The cough may resemble the whoop of pertussis, but differs in its persistence and the absence of contagion. It is rare to have any physical signs from this condition; if present they are similar to those described for tuberculosis of the mediastinal lymph nodes. Treatment, aside from measures directed against the primary condition, should be directed along the lines of general hygiene.

**Pigmentation and Sclerosis.**—In our civilization pigmentation of the mediastinal lymph nodes is an almost constant occurrence except in the very young. Carbon deposits are usually present in the peribronchial lymph nodes, and this is very marked in those whose daily occupation exposes them to a coal-dust laden atmosphere. The same conditions prevail for other occupations with similar exposure, as stone cutting and cutlery grinding. Other forms of pathological pigmentation occur, but are of very minor importance. Frequently the pigment deposits show a curious lack of uniformity of distribution, both in lymph-node groups and in individual lymph nodes, which is difficult of explanation.

In the great majority of persons this pigmentation produces no injury. If the condition is marked the lymph nodes are slightly enlarged and somewhat sclerosed, but this ordinarily produces no symptoms. Possibly a few cases of persistent cough may be due to the irritation of the bronchial mucous membrane by slightly enlarged lymph nodes.

In some a more extensive chronic inflammation is set up with induration of the surrounding tissues and adhesions, which may lead to pressure on or perforation into mediastinal structures. Very often traction diverticula, especially those of the œsophagus, seem to be due primarily to the adhesion of sclerosed pigmented glands.

Softening and breaking down of the pigmented nodes may occur with perforation of adjacent viscera or abscess formation. A number of such cases have been reported. Sternberg[1] found 34 of these cases in 6132 autopsies. In most of them the bronchus, alone or with other viscus, had

[1] *Verhandl. d. Deutsch. path. Gesellschaft*, September, 1905, 309.

been perforated and putrid bronchitis and pulmonary gangrene produced. All of Sternberg's cases were in individuals between forty and eighty-one years of age. However it is not always clear that these are due to the pigmentation and sclerosis alone, and it is probable that in some at least syphilis and tuberculosis have been factors. Sternberg regarded the cases cited above as having their cause in the anthracosis. Chiari, on the other hand, stated in the discussion of this paper that he considered the majority of cases of this type as primarily of tuberculous origin. The symptoms produced by these changes are almost entirely the result of the adhesions with or without perforation and need no special discussion here.

**Tuberculosis.**—Tuberculous lesions in the mediastinal lymph nodes are very common. In most cases they are associated with pulmonary tuberculosis or tuberculous caries of the vertebræ, ribs, or sternum. In a smaller number of cases the tuberculosis appears to be primary in the mediastinal lymph nodes; at least, that is the most prominent and most advanced tuberculous lesion of the body. This last form occurs especially in children.

In the mediastinal lymph nodes various tuberculous lesions occur. Of these there are three general groups—miliary tuberculosis, caseation and calcification with moderate enlargement, and proliferative lesions with tumor formation. Miliary tuberculosis occurs in its typical form, producing slight gross changes. Much more common is caseation and calcification in lymph nodes of normal or moderately enlarged size. In these, reactive connective-tissue changes with sclerosis are common. The clinical importance of this second group is threefold: they form a source for tuberculous infection of other organs; by extension they produce mediastinal abscesses; they rupture into adjacent structures, bronchi, trachea, œsophagus, veins, arteries, or pericardium, with serious consequences. Apart from these the local process is practically symptomless.

Numerous cases might be cited of acute general miliary tuberculosis resulting from a chronic lesion in the mediastinal lymph nodes. They are quite common in the experience of all who make postmortem examinations. In a recent case of acute tuberculous meningitis, seen at the Massachusetts General Hospital, the only discoverable chronic tuberculous lesion was in the mediastinal lymph nodes, which were caseous and considerably enlarged. During life they had produced no symptoms. Mediastinal abscess of tuberculous origin has already been discussed.

Numerous cases of perforation of caseous tuberculous glands have been reported in the literature. In a Boston City Hospital autopsy a broken-down tuberculous lymph node, 1.5 cm. broad and several cm. long, had perforated into the left bronchus near the tracheal bifurcation. More interesting are the cases where tuberculous lymph nodes lead to a fistulous communication between a bronchus and a bloodvessel. Kidd[1] reports a case of fatal hæmoptysis in a girl of fifteen where there was such a communication with the pulmonary artery.

Extension from a lymph node to the aorta may be a source of general miliary tuberculosis. In a Boston City Hospital case, reported by Councilman[2] adhesion of a small caseous node to the aorta produced first a small aneurism and secondarily a general miliary tuberculosis. A somewhat

[1] *Transactions of the Pathological Society of London*, 1885, xxxvi, 102.
[2] *Medical and Surgical Reports of Boston City Hospital*, 1896, vii, 216.

similar case is given by Liefmann.[1] In the latter there was considerable hemorrhage into the space formed by the broken-down lymph nodes.

Rupture into a bronchus or the trachea may occur without immediately serious results. However, rupture is sometimes immediately fatal, as in a case of Voelcker,[2] in which a child of five, previously in good health, died suddenly and at autopsy a portion of a caseous bronchial lymph node was found obstructing the aperture of the glottis. This mass had entered the respiratory tract through a perforation in the right bronchus. Several similar cases have been reported by Parker, Westcott, Kelynack, and others.

Rupture into the œsophagus is less common than into the bronchi and trachea. Rupture into the pericardium or pleura with subsequent tuberculous inflammation of these cavities may occur. Fistulous communication with the cutaneous surface may be formed, or with this may be combined perforation of a bronchus or the œsophagus, so that air or food may be expelled from the skin sinus.

The proliferative tuberculous lesions of the mediastinal lymph nodes are not so frequent as the two forms previously discussed, but as a group they are of rather more clinical importance, since with them the lymph nodes form definite tumor masses which may or may not caseate. This form occurs in adults, but is much more common in children, in whom it forms an important group of tuberculous cases. Here we have large masses of tissue in the mediastinum, composed of enlarged lymph nodes, bound together more or less firmly by connective tissue, and producing many of the pressure symptoms already described for tumors.

**Symptoms.**—In many cases of tuberculosis of the mediastinal lymph nodes no symptoms result. In children dying of some of the acute infectious diseases tuberculous lymph nodes are quite frequently found without there having been any symptoms during life pointing to them. When the lymph nodes are sufficiently enlarged and so situated as to produce pressure, we get a variety of symptoms. A very important one is cough due to bronchial irritation. This is apt to be persistent in the form of paroxysms of spasmodic cough, often resembling pertussis. Substernal pain may occur. More characteristic is pain behind, in the region of the fourth dorsal vertebra. Dyspnœa may be present, as also dysphagia. The latter may be present and persist without the œsophageal sound giving any evidence of stenosis. Venous dilatation, œdema, cyanosis, hoarseness, and aphonia, as evidence of localized intrathoracic pressure, occur.

**Physical Examination** is often negative. In some cases enlarged lymph nodes can be palpated in the suprasternal notch. Fixation of the trachea during respiration may be detected. In a few cases dulness on percussion is elicited, especially behind in the region of the second to sixth dorsal vertebræ on one or both sides, near the midline or in front over the sternum. In other cases, with or without dulness near the midline behind, percussion over the spinous processes may give resonance different from that elicited under normal conditions. Korányi[3] has pointed out that normally over the seventh cervical spine there is flatness; from the first to fifth dorsal spines there is a gradually increasing resonance, and, from the sixth to the

[1] *Centralbl. f. allg. Path.*, etc., 1904, xv, 749.
[2] *Transactions of the Pathological Society of London*, 1898, xlix, 22.
[3] *Zeit. f. klin. Med.*, 1906, lx, 295.

eleventh, resonance. In cases with enlarged bronchial lymph nodes flatness continues below the seventh cervical and modified resonance extends to a lower level than in the normal. On auscultation increased transmission of respiration and voice may be detected in these regions.

Smith has called attention to a venous hum, heard over the sternum with the head thrown back, as a sign of enlarged bronchial lymph nodes. Wiederhofer attaches importance to a relatively loud expiration heard behind over the left bronchus, where normally sound transmission is rather less than on the right.

Neisser[1] has recently devised an ingenious method for palpating the bronchial lymph nodes. He uses a stomach tube with a thin rubber membrane so tied over its lateral opening that, when air is forced into the tube, the rubber membrane is blown up to produce a local bulging. The tube is passed into the œsophagus so that the lateral opening is about at the level of the bifurcation of the trachea. Air is now forced into the stomach tube and pressure is brought to bear on the wall of the œsophagus by the dilating rubber membrane. In consequence pressure is made on the wall of the œsophagus in the region of the bronchial lymph nodes. If the latter are in an inflammatory condition pain is produced by this pressure, and Neisser considers this a delicate method for detecting disease of the bronchial lymph nodes. This may prove of service in diagnosing even the slighter forms of tuberculosis of the bronchial lymph nodes.

**Diagnosis.**—Diagnosis in children in whom tumors are not so very common can be correctly made in many cases. In adults the difficulties are much greater, since, frequently, all the signs of tumor are closely simulated, and this diagnosis is made on account of the greater frequency of mediastinal tumors in the adult. Even confusion with aneurism may arise.

**Treatment.**—The treatment does not differ from that applicable to other forms of tuberculosis unsuited for surgery.

[1] *Deutsch. Arch. f. klin. Med.*, 1905, lxxxvi, 28.

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